

Electrochemical Dealkylation of Aliphatic Tertiary and Secondary Amines

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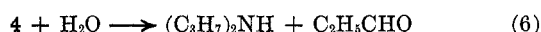
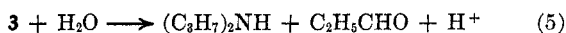
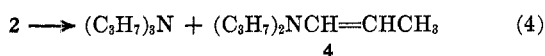
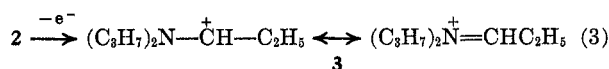
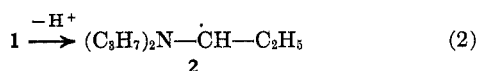
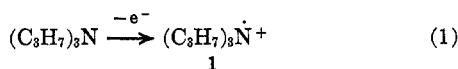
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Previous work has indicated that straight-chain aliphatic amines undergo dealkylation after anodic oxidation, either by hydrolysis of the enamine formed in a one-electron process, or by hydrolysis of the iminium salt formed in a two-electron process. In the present work, evidence is presented in favor of the enamine as the intermediate. In the earlier work, secondary amines were oxidized but dealkylation was not observed. This has been shown to be incorrect; the reaction of di-*n*-propylamine is very similar to that of tri-*n*-propylamine. It is suggested that electrolytic dealkylation of simple aliphatic amines is a general reaction which can lead from tertiary to secondary and primary amine and finally to ammonia and elemental nitrogen.

Accounts of detailed examinations of the anodic oxidation of primary and tertiary aliphatic amines have been published previously.^{1,2} Straight-chain primary amines were found to undergo scission of the carbon-nitrogen bond which resulted in formation of ammonia, elemental nitrogen, protons, and an aldehyde having the same number of carbon atoms as the amine taken. Condensation products which would be expected from a mixture of primary amine and aldehyde were found. Two reaction schemes were suggested. One involved a two-electron formation of an iminium ion which hydrolyzed; the other involved decomposition of the initially formed ion radical.

Tertiary amines were found to undergo dealkylation to the corresponding secondary amine and the appropriate aldehyde. The reaction scheme proposed is outlined in eq 1-6, using tri-*n*-propylamine as the ex-

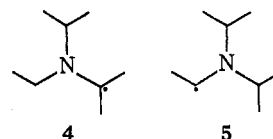


ample. This reaction scheme led to predictions of product identities and yields which were in reasonable agreement with experimental results, provided that it was assumed that the secondary amine produced also underwent anodic oxidation. The reaction scheme consists of an initial electron transfer followed by proton loss to form the neutral radical 2, which could either lose an electron to form the iminium salt 3, or disproportionate to form the enamine 4. Either of these would be expected to hydrolyze to give the products that are found. Furthermore, the stoichiometry is the same for either type of reaction; accordingly, on the basis of the information available, no distinction could be made between these two schemes.

It was suggested, however, that, on examining the results obtained by oxidizing unsymmetrically substituted tertiary amines, a mechanism involving an enamine intermediate appeared to be plausible in cer-

tain cases. Reaction of benzyldimethylamine and dibenzylmethylamine resulted mainly in loss of the benzyl group rather than the methyl group. It would be predicted, on the basis of radical stability, that this would occur because of preferential loss of benzylic protons in step 2. Steps 3 and 5 would then follow. Oxidation of allyldiethylamine produced primarily diethylamine, indicating preferential loss of the allyl group. This also would be predicted on the same basis.

When this line of reasoning is extended to the cases of di-*i*-propylethylamine, dicyclohexylethylamine, or cyclohexyldiethylamine, incorrect predictions are obtained. One would expect that reactions analogous to steps 1 and 2 would produce, preferentially, radical 4 from diisopropylethylamine, rather than radical 5.



However, this would logically lead to loss of an isopropyl group. In fact, loss of the ethyl group is strongly favored. Similarly, an ethyl group is lost in preference to the cyclohexyl group, contrary to predictions based upon radical stabilities. It may be noted that predictions based upon radical stabilities work out only in those cases which involve groups which would form especially stable radicals. This suggests that a different mechanism may be operating in the other cases. One possibility is that the enamine intermediate may be involved in the other cases. It may be noted that the one example studied which can neither form an enamine nor an especially stable radical, trimethylamine, apparently does not undergo simple dealkylation.

In the examinations of tertiary and primary amine oxidation, a degree of similarity was found in that reactions lead to cleavage of carbon-nitrogen bonds with formation of the less highly substituted amine or ammonia, and the appropriate aldehyde. It was noted, however, that no dealkylation was observed upon oxidation of dipropylamine. Apparently the reaction of secondary amines was significantly different from those of tertiary and primary amines.

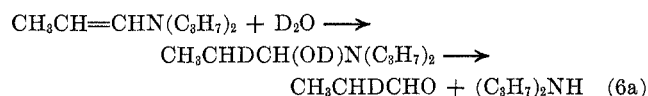
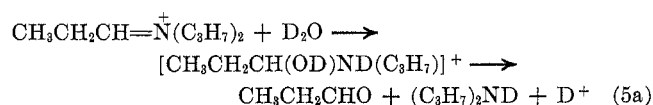
The present work was undertaken in order to get a better understanding of the dealkylation process and to inquire into the anodic reactions of secondary aliphatic amines. As a result, we believe that it can be shown that the process of electrochemical dealkylation in straight-chain aliphatic amines is a very general one

(1) K. K. Barnes and C. K. Mann, *J. Org. Chem.*, **32**, 1474 (1967).(2) P. J. Smith and C. K. Mann, *ibid.*, **34**, 1821 (1969).

leading, in principle, from a tertiary amine through the secondary and primary amines to ammonia and finally to nitrogen gas, together with appropriate aldehydes. We believe further that there is now convincing evidence for the involvement of the enamine as the intermediate in electrochemical dealkylation.

Results and Discussion

Dealkylation Mechanism.—In the earlier work,² it was demonstrated that dealkylation to aldehyde and amine occurs only in the presence of at least small amounts of water; accordingly, the hydrolyses in steps 5 and 6 were included. It may be noted that, while the stoichiometry is the same for either process, the actual mechanism of incorporation of water in the reactions that are summarized in steps 5 and 6 would be different. These reactions with deuterium oxide, rather than water, are outlined in steps 5a and 6a. They differ in



that aldehyde produced by reaction of enamine with D₂O would show deuterium at the α position, while that from the iminium salt would have hydrogen in that position.

To check this point, the oxidation of both tripropylamine and dipropylamine was carried out in a rigorously dried system to which a small amount of D₂O had been added. The aldehyde produced was recovered, purified, and examined by mass spectroscopy, nmr, and ir spectroscopy. In addition, the 2,4-dinitrophenylhydrazones were prepared. The mass spectrum of the aldehyde recovered from electrolysis of either amine with D₂O showed a molecular weight of 59, indicating inclusion of one deuterium. This aldehyde formed a 2,4-dinitrophenylhydrazone with a molecular weight of 239, also indicating monodeuteration. The nmr spectrum of the deuterated aldehyde exhibited a peak for the aldehyde proton at the chemical shift and in the intensity expected for propionaldehyde. Instead of the quartet and triplet shown by the ethyl group of propionaldehyde, very complex groups of peaks with 1.1-Hz splitting were observed, centered about the same chemical shifts exhibited by the methyl and methylene groups of propionaldehyde. This indicates that deuteration has occurred either at the 2 or the 3 position.

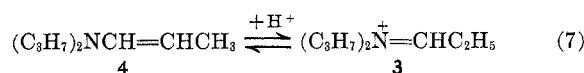
The infrared spectrum of the deuterated aldehyde contained peaks assigned to asymmetric methyl stretch and carbon-hydrogen stretch of the aldehyde function which occurred at the same frequencies as did these peaks in the propionaldehyde spectrum. In propionaldehyde, the symmetric stretch vibrations for both methyl and methylene occur at the same frequency. For the deuterated compound, a peak at this frequency occurred, but it showed lower intensity relative to other peaks in the spectrum than was the case for propionaldehyde. The peaks for CH₂ asymmetric stretch and for CH₂ wag, both present in the spectrum of propionaldehyde, are absent from the spectrum of

the deuterated sample. All assigned frequencies fall within the expected ranges for the expected frequencies.³ In addition, when compared with the vapor phase spectrum of propionaldehyde, for which assignments have been made,⁴ the spectra correspond except that all peaks in the liquid phase spectra are shifted 10–30 cm⁻¹ toward longer wavelengths relative to those in the vapor phase spectrum.

These data show that the aldehyde recovered from electrolyses made in the presence of D₂O is deuterated in the 2 position. If this is to be considered evidence in favor of a particular mechanism, there must be assurance that deuteration did not simply take place by exchange between D₂O and ordinary propionaldehyde. This reaction has been studied by Hine, *et al.*,⁵ who demonstrated that aliphatic amines catalyze hydrogen-deuterium exchange in the aldehydes. They pointed out, however, that the exchange reaction is not an effective preparative route to the deuterated aldehyde. Attempts to prepare deuterated aldehyde by shaking the pretreated compound with a concentrated solution of amine in D₂O gave only about a 33% yield. Our examination shows that the monodeuterated aldehyde is formed in the electrolysis virtually to the exclusion of ordinary aldehyde, indicating that some mechanism other than H–D exchange is operating. Our reaction 6a does, in fact, resemble the reaction actually used by Hine, *et al.*, to produce the deuterated aldehyde that they used as starting material.

While the possibility of H–D exchange during electrolysis is precluded, there could be a question about exchange during the separation procedure which includes a distillation. This was checked by performing the separation, starting with propionaldehyde in acetonitrile with D₂O added. Mass spectroscopic examination showed no appreciable deuterium enrichment above the natural abundance. We therefore conclude that propionaldehyde-2-*d* is produced during the electrolysis of both tripropylamine and dipropylamine and that H–D exchange is not responsible for its formation.

In considering the dealkylation process, it must be noted that enamine and iminium ion should be in equilibrium as indicated in eq 7. Furthermore, it



would be expected by analogy from cyclic tertiary amines⁶ that the enamine would be a significantly stronger base than the corresponding saturated amine.

In our experiments, the solution initially contains the saturated amine which is gradually protonated. If an equilibrium were established involving tripropylamine, tripropylammonium ions, enamine **4**, and iminium ions **3**, it would be shifted toward a mixture of **3** and tripropylamine. If **3** were formed as a result of reactions 1–3 then there would be no opportunity for enamine to be formed, because the system contains no base stronger than the enamine. Since we do have evidence that the enamine is being dealkylated, it therefore follows that the iminium salt is not being

(3) C. N. R. Rao, "Chemical Applications of Infrared Spectroscopy," Academic Press Inc., New York, N. Y., 1963.

(4) E. F. Worden, *Spectrochim. Acta*, **18**, 1121 (1962).

(5) J. Hine, J. G. Houston, J. H. Jensen, and J. Mulders, *J. Amer. Chem. Soc.*, **87**, 5050 (1965).

(6) R. Adams and J. E. Mahan, *ibid.*, **64**, 2588 (1942).

formed either by reaction 3 or 7. We suppose that this indicates that reaction 4 is much faster than reactions 2 and 3 and that reaction 6 is faster than reaction 7.

The recoveries of amines in the present and previously reported work were never quantitative; for example, for tripropylamine it amounted to 80–95% based upon nitrogen in the starting amine. Reaction solutions showed a uv absorption at 315 nm. When water concentration was held below 5 mM, it was noted that this uv band was more intense. The material responsible for the 315-nm band was isolated as a gum from the nonvolatile fraction of the reaction mixture by CHCl_3 extraction and thin layer chromatography. Taken from the reaction mixture without having been made basic, it showed a sharp and intense ir absorption at 1695 cm^{-1} . If the material was made basic during the isolation, this peak was shifted to 1660 cm^{-1} . It is characteristic of α,β -unsaturated tertiary amines to show a peak at around 1650 cm^{-1} which shifts 20–50 cm^{-1} toward higher frequencies when the salt is prepared.⁷ This behavior has been attributed to a transformation of the type indicated in eq 8. Mass spectra of these samples showed groups of peaks with about 14 mass units separation between adjacent maxima which exhibited a regular diminution in intensity to merge with background noise above m/e of 310.

We are unable to specify the structure of the high-molecular-weight product, the presence of which was mentioned in the previous report.² We suggest that it is formed from the enamine, perhaps by condensation with aldehyde, and, in the presence of dipropylammonium ions in the latter stages of the reaction, is converted to the salt form. Presumably stabilized by the condensation against C–N scission, it is capable of undergoing the enamine–salt conversion analogous to those shown by cyclic amines.

It is of interest to note that several examples of enamine formation by chemical oxidation of aliphatic amines have been reported. Leonard and coworkers⁸ studied the mercuric acetate oxidation of a wide variety of monocyclic, bicyclic, and tetracyclic tertiary amines. In general, the products showed α,β -unsaturation and, because they were cyclic compounds, they could be readily isolated and identified. Henbest and coworkers have reported the production of enamines by MnO_2 ,⁹ benzoyl peroxide,¹⁰ and quinone¹¹ oxidation of aliphatic secondary and tertiary amines. They were detected by forming colored condensation products with halogenated quinones.

Anodic Oxidation of Secondary Amines.—To investigate the differences in reactions of simple tertiary and secondary aliphatic amines, an examination of the behavior of di-*n*-propylamine was carried out. In addition to the experiments described above which show that aldehyde is produced and that an enamine intermediate is involved for both tertiary and secondary amine dealkylations, an examination of the reaction products was undertaken. The product mixture was shown to contain dipropylammonium and *n*-propylammonium ions and propionaldehyde. These com-

pounds were identified by comparing their retention times, on two different glpc columns, each run at three different temperatures, with those of valid samples. In addition, nmr spectra of samples of the amine perchlorates were shown to be identical with those of valid samples. The uv spectrum of the 2,4-dinitrophenylhydrazone was identical with that shown in the Sadtler Laboratories collection, No. 1194, Vol 4. As mentioned above, the hydrazone from the deuterated aldehyde had a molecular weight of 239, to be expected for the derivative of monodeuterated propionaldehyde. Some quantitative results are presented in Table I. In

TABLE I
PRODUCT ANALYSIS AFTER REACTION OF DI-*n*-PROPYLAMINE^a

Potential ^b	<i>n</i>	% EtCHO ^c	% $\text{Pr}_2\text{NH}_2^+ \text{c}$	% Pr-NH ₃ ⁺
1.40	0.88, 0.90	25.4, 25.3	16.4, 16.9	49
1.00	0.83, 0.85	19.6, 19.0	9.9, 10.4	66

^a Initial amine concentration = 17 mM in 0.10 M NaClO_4 -MeCN, initial water concentration = 500 mM. ^b Volts vs. Ag–AgNO₃ (0.10 M). ^c Mole per cent of starting amine.

addition to these, the products included components which show uv absorption at 226 nm and at 315 nm. That responsible for the 315-nm absorption is discussed above. It was formed in much larger concentrations in reactions carried out at +1.00 V than in those run at +1.40 V. We assume that this material reacts further at the higher potentials. The compound responsible for the 226-nm absorption was isolated and identified as 2-methyl-2-pentenalpropylamine. This compound was shown to be one of the products of oxidation of *n*-propylamine.¹ It is formed in much larger concentrations from reaction at +1.40 V than at +1.00 V.

The results described here indicate that the reaction of dipropylamine in the presence of small concentrations of water is fundamentally similar to that of tripropylamine. The reaction causes dealkylation to form primary amine, propionaldehyde, and protons. The enamine is involved in a hydrolytic dealkylation step as it is in the reaction of tripropylamine. Therefore, it is possible in principle to perform an electrochemical degradation, starting with a simple tertiary aliphatic amine and proceeding stepwise through the secondary amine, the primary amine, and ammonia to elemental nitrogen together with the aldehydes and protons formed in each of the steps. In practice, the formation of unreactive protonated amine greatly reduces the yield in each successive step. Starting with tripropylamine in acetonitrile, together with enough water to assure that the dealkylation steps analogous to reaction 6 can occur, only a very small yield of *n*-propylamine and no ammonia can be detected in the product mixture.

Experimental Section

Reagents.—The amines used were Eastman White Label, used as received after glpc examination showed them to have no apparent significant amounts of impurities. The solvent and supporting electrolyte were prepared as described previously.²

Procedures.—The electrolysis apparatus and procedures were similar to those previously described.² Electrolyses were carried out in H-type cells at perforated cylindrical platinum anodes. Taking the geometrical area of only the exterior of the anode as

(7) N. J. Leonard and V. W. Gash, *J. Amer. Chem. Soc.*, **76**, 2781 (1954).

(8) N. J. Leonard and coworkers, *ibid.*, **80**, 371 (1958), and preceding papers.

(9) H. B. Henbest and A. Thomas, *J. Chem. Soc.*, 3032 1957.

(10) D. Buckley, S. Dunstan, and H. B. Henbest, *ibid.*, 4880 1957.

(11) H. B. Henbest and P. Slade, *ibid.*, 1558 1960.

a measure of the effective electrode area, current density at the outset of a typical experiment amounted to 9.8 mA/cm². This decreased continuously during the experiment to a constant value of 9 μ A/cm². Product analyses for Pr₂NH, PrNH₂, and Et-CHO were performed by glpc using Dowfax 9N9 with NaOH and also Carbowax 20M as liquid phases. These were repeated at 75, 100, and 150°.

Identification of Propionaldehyde-2-d.—A 150-ml MeCN solution, 0.25 *M* in NaClO₄, 230 mM in D₂O, and 50 mM in dipropylamine, was electrolyzed at a Pt anode at +1.00 V vs. Ag-AgNO₃ (0.10 *M*). The product mixture was distilled through a spinning-band column, the first 12 ml of distillate being taken at 72–74°. This fraction was redistilled with the separation efficiency monitored by glpc. A 2-ml cut contained most of the aldehyde; it was further fractionated by glpc, using a Carbowax 20M column at 100°. The aldehyde fraction was trapped and taken up in CDCl₃ for nmr and ir examination. A sample of propionaldehyde in MeCN was subjected to the same separation to ascertain that the separation procedure was not causing exchange. There was indication that some of the aldehyde was lost because of condensation at various stages.

The mass spectra were obtained by distilling some of the concentrated solution produced from the spinning-band column into the spectrometer inlet system while the fraction was maintained below ice temperature. It was ascertained, using a sample of propionaldehyde in MeCN of the appropriate concentration, that the molecular ion of the aldehyde is observed by this procedure. However, the solvent peaks obscure the fragmentation pattern of the aldehyde.

Preparation of 2-Methyl-2-pentenalpropylamine.—A sample of this product was prepared to provide a comparison with the electrolytically generated material by the procedure previously described.¹

Registry No.—Di-*n*-propylamine, 142-84-7.

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Mechanism of the Ferricyanide-Catalyzed Chemiluminescence of Luminol

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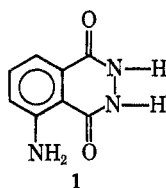
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A study of the mechanism of the potassium ferricyanide chemiluminescent oxidation of luminol (5-amino-2,3-dihydro-1,4-phthalazinedione) is reported. An important feature of the proposed mechanism is the one-electron oxidation of the luminol dianion by ferricyanide to 5-aminophthalazine-1,4-semidione. The semidione intermediate may react with oxygen to produce electronically excited 3-aminophthalic acid and nitrogen. Alternatively, the semidione may be further oxidized by ferricyanide in a nonluminescent reaction.

In chemiluminescent systems, the rate of formation of the excited state is given by

$$d[x]/dt = i/\phi \quad (1)$$

where *x* is the luminescing molecule, ϕ the quantum yield for fluorescence of *x*, and *i* the intensity of emitted light. Thus, in systems where ϕ does not change during the reaction, the intensity is a measure of the rate of reaction. We have used this relationship to study the mechanism of the potassium ferricyanide oxidation of luminol (5-amino-2,3-dihydro-1,4-phthalazinedione, 1) in aqueous base.



The chemiluminescence of luminol has been the subject of numerous investigations.¹ The mechanism of the reaction in aqueous dimethyl sulfoxide has been studied by White.² The role of ferricyanide as a catalyst has been explored;³ however, the exact mechanism of its action has not been elucidated.

We studied the kinetics of the reaction in order to clarify the role of ferricyanide in this oxidation. The chemiluminescence with ferricyanide as a catalyst has

generally been studied in the presence of hydrogen peroxide. In order to simplify analysis of the kinetics we have studied the reaction in the absence of peroxide.

Experimental Section

Materials.—Commercially available luminol was used without further purification. When the sodium salt of luminol,⁴ which had been recrystallized from water, was used, the results were unchanged. All other reagents were of analytical grade and were not further purified. All solutions used were freshly prepared.

Light Intensity Measurements.—The reaction vessel was a test tube (15 × 150 mm) placed in a light-tight compartment provided with a shutter opening to an RCA IP21 phototube. The output voltage from the phototube was displayed on a Varian recorder as a function of time. The apparatus was calibrated with a standard luminol reaction by the method of Lee and Seliger⁵ so that the intensity was reported in photons second⁻¹.

A solution of luminol (3.0 ml) in aqueous sodium hydroxide was placed in the test tube, and the reaction was initiated by injection of a potassium ferricyanide solution (0.3 ml). A stream of air was bubbled continuously through the reacting solution. This air stream ensured that the solution was kept saturated with oxygen and that mixing of the reactants was rapid. The rate of mixing appears to be fast compared to intensity decay; changing the rate of air flow into the solution did not alter the initial intensity of emitted light.

A Y-shaped reaction vessel equipped with a vacuum stopcock was used to measure intensity as a function of pressure. The luminol solution (3.0 ml) was placed in one arm of the vessel, and the ferricyanide solution (0.3 ml) in the other. The solutions were degassed, and air was introduced at known pressure. The vessel was placed in a light-tight box, and the reaction was

(1) E. H. White, "Light and Life," W. D. McElroy and B. Glass, Ed., Johns Hopkins Press, Baltimore, Md., 1961, p 183.

(2) E. H. White, O. Zafiriou, H. M. Kagi, and J. H. M. Hill, *J. Amer. Chem. Soc.*, **86**, 940 (1964); E. H. White and M. M. Bursley, *ibid.*, **86**, 941 (1964).

(3) F. H. Stross and G. K. Branch, *J. Org. Chem.*, **3**, 385 (1938).

(4) E. H. Huntress, L. N. Stanley, and A. S. Parker, *J. Chem. Educ.*, **11**, 241 (1934).

(5) J. Lee, A. S. Westley, J. F. Ferguson, III, and H. H. Seliger, in "Bioluminescence in Progress," F. H. Johnson and Y. Haneda, Ed., Princeton University Press, Princeton, N. J., 1966, p 35.