Reactions of Pyridinium Salts with Alkaline Hydrogen Peroxide. Formation of Pyrrolidinone Hydroperoxides from 1-Methyl- and 1-Benzyl-3-carbamoylpyridinium Chloride[1,2]

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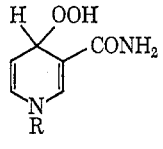
An attempt to prepare a hydroperoxide adduct of 1-methyl- (or 1-benzyl-) 3-carbamoylpyridinium chloride by treatment of the salt with alkaline hydrogen peroxide results in the formation of pyrrolidinone hydroperoxides, **2a** and **2b**, the end products of an extensive rearrangement. Yields are low (7–8%), but the products are obtained in good purity from readily available starting materials. The structure of the hydroperoxide derived from the 1-methyl salt was established by its conversion to N-methyl-N-[(1-methyl-2-oxo-3-pyrrolidinyl)methyl]formamide (**6**), which was synthesized independently from 1-methyl-2-pyrrolidinone. The structure of the corresponding pyrrolidinone from the 1-benzyl salt is inferred from its physical and chemical similarities to the methyl derivative. Treatment of 1-benzyl-3-acetylpyridinium chloride with alkaline hydrogen peroxide gives N-benzylformamide in low yield, and similar treatment of the 3-bromo derivative gives N-benzyl-2,2-dibromoacetamide, also in low yield. The infrared, ultraviolet, nmr, and mass spectra of the new pyrrolidinone derivatives are discussed, and a possible mechanism for the rearrangement is presented.

In a study of the reducing properties of 1-benzyl-1,4-dihydronicotinamide, a model for the coenzyme NADH (reduced nicotinamide–adenine dinucleotide), the oxidation of cyclobutanone to butyrolactone and butyric acid in low yield was observed in the presence of oxygen and the dihydronicotinamide.[3] No reaction occurred in the absence of oxygen or the nicotinamide derivative. When the bright lemon-yellow dihydronicotinamide was exposed to air, it became orange; this orange material when treated with cyclobutanone also gave butyrolactone and butyric acid. The dihydronicotinamide apparently is acting as an oxygen carrier in the reaction, and, because of the importance of oxidations in living systems in which the pyridine coenzymes play a role,[4] the identification of oxygen-rich intermediates derived from the coenzyme model was attempted. A possible intermediate in the reaction of oxygen, cyclobutanone, and 1-benzyl-1,4-dihydronicotinamide is a hydroperoxide of dihydronicotinamide such as 4-hydroperoxy-1-alkyl-1,4-dihydronicotinamide, **1**.[5] An attempt to synthesize such an intermediate by the reaction of the pyridinium salt with hydroperoxide anion was unsuccessful, but a new, stable hydroperoxide was obtained which may be of interest in possible metabolic paths for the degradation of the pyridine coenzymes in the presence of cellular hydrogen peroxide.[6]



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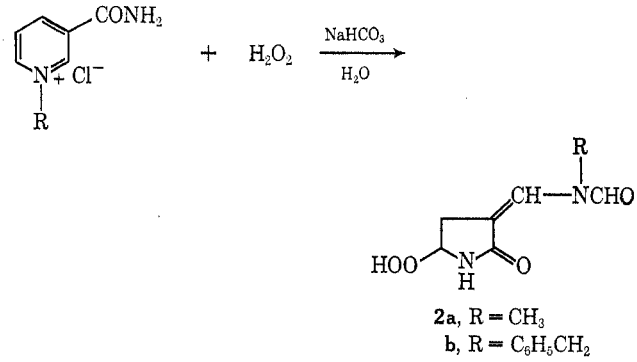
Treatment of 1-Methyl- or 1-Benzyl-3-carbamoylpyridinium Chloride with Alkaline Hydrogen Peroxide.—A white solid of molecular formula $C_7H_{10}N_2O_4$ or $C_{13}H_{14}N_2O_4$ precipitated slowly (1–3 months for the former, 6 days for the latter) when 1-methyl- or 1-benzyl-3-carbamoylpyridinium chloride, respectively, was treated with excess 30% hydrogen peroxide and 1 equiv of sodium bicarbonate at 0–5°. The compounds are hydroperoxides: they oxidize iodide ion to iodine, show absorption in the infrared at 837–841 cm^{-1} for a hydroperoxy group,[7] show a base peak in the mass spectrum caused by loss of hydrogen peroxide plus carbon monoxide, and show absorption in the nmr spectrum at δ 11.54–11.56 (dimethyl sulfoxide-d_6).[8] The structures of the hydroperoxides were shown to be **2a** (N-



2a, R = CH_3
b, R = $C_6H_5CH_2$

(1) This work was aided by Grant AM-07770 of the National Institutes of Health, U. S. Public Health Service, which we acknowledge with gratitude.

(2) For complete details, see D. W. Bristol, Ph.D. Thesis, Syracuse University, 1969. Also see D. W. Bristol and D. C. Dittmer, Abstracts, 158th National Meeting of the American Chemical Society, Division of Organic Chemistry, New York, N. Y., Sept 1969, No. 150.

(3) D. C. Dittmer, R. A. Fouty, and J. R. Potoski, *Chem. Ind.* (London), 152 (1964).

(4) "Oxygenases," O. Hayaishi, Ed., Academic Press, New York, N. Y., 1962.

(5) Recently, **1** was proposed as a possible intermediate in the reaction of 1-benzyl-1,4-dihydronicotinamide with oxygen in the presence of phenazine or cupric ions: L. S. Negievich, O. M. Grishin and A. A. Yasnikov, *Ukr. Khim. Zh.*, **34**, 381 (1968); *Chem. Abstr.*, **69**, 76221 (1968).

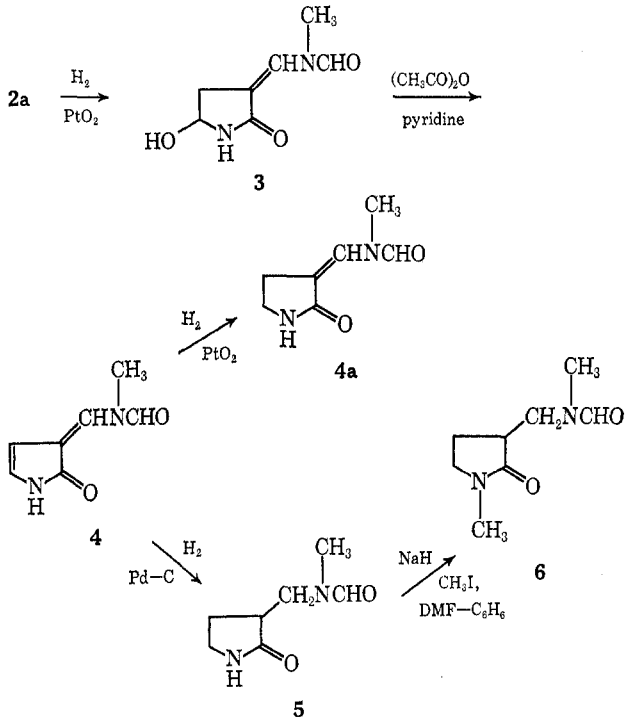
(6) Organic peroxides inhibit the growth of ascites tumors: C. Weitzel, E. Buddecke, F. Schneider, and H. Pfeil, *Z. Physiol. Chem.*, **325**, 65 (1961); B. Weitzel, E. Buddecke and F. Schneider, *ibid.*, **323**, 211 (1961).

(7) B. F. Sagar, *J. Chem. Soc., B*, 428 (1967).

(8) Loss of hydrogen peroxide is observed in the mass spectra of simple hydroperoxides: A. R. Burgess, R. D. G. Lane, and D. K. Sen Sharma, *ibid., B*, 341 (1969). A nmr spectrum of cumene hydroperoxide in dimethyl sulfoxide-d_6 has absorption at δ 11.2. Two N-alkylamide hydroperoxides show absorption at δ 10.80 in acetone-d_6 (ref. 7).

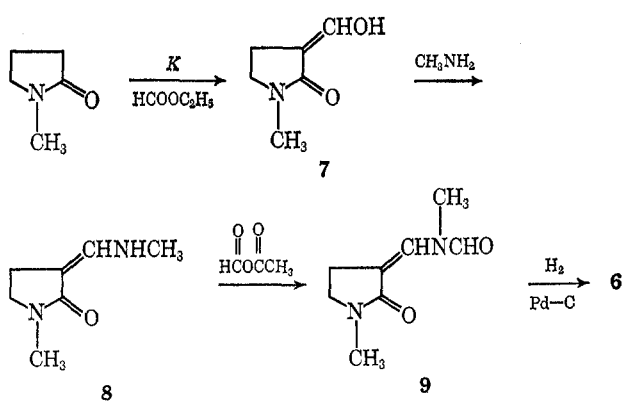
[(5-hydroperoxy-2-oxo-3-pyrrolidinylidene)methyl]-N-methylformamide)[9] and **2b** (N-benzyl-N-[(5-hydroperoxy-2-oxo-3-pyrrolidinylidene)methyl]formamide or 3-benzylformamidomethylene-5-hydroperoxy-2-pyrrolidinone). The structure of the N-methyl derivative **2a** was deduced from its conversion to saturated pyrrolidinone **6** coupled with an independent synthesis of **6**. The structure of **2b** was deduced from physical and chemical analogies to **2a**. The degradation scheme of **2a** is outlined in Scheme I, and an independent synthe-

SCHEME I



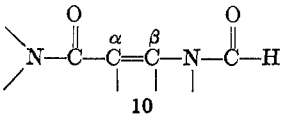
sis of **6** from 1-methyl-2-pyrrolidinone is given in Scheme II. Pertinent points about the degradation,

SCHEME II



synthesis, and the physical properties of this class of pyrrolidinone derivatives are discussed below.

Properties of Hydroperoxides 2a and 2b.—The β-formamido-α,β-unsaturated amide group **10** occurs not only in the hydroperoxides but also in compounds **3, 4, 4a,** and the N-benzyl analog of **3**. All of these



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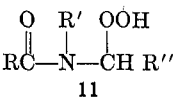
derivatives show intense ultraviolet absorption near 264 mμ (ε ~ 20,000) and characteristic infrared absorption around 1700–1720 (formyl carbonyl stretching vibration), 1671–1695 (pyrrolidinone carbonyl), and 1620–1635 cm^{-1} (carbon–carbon double bond).[10]

The average absorptions (δ) of the protons of **2a** observed in the nmr spectrum (dimethyl sulfoxide-d_6) are summarized in structure A. Those of **2b** are similar except for upfield shifts for the C-4 protons, and downfield shifts for the formyl and vinyl protons. The chemical shift of the 5-methine proton at δ 5.33 is comparable with the average value of δ 5.48 for the methine proton in N-alkylamide hydroperoxides **11**[7] indicates that the hydroperoxy group is at the 5 position rather than at the 4 position. Frequency sweep double res-



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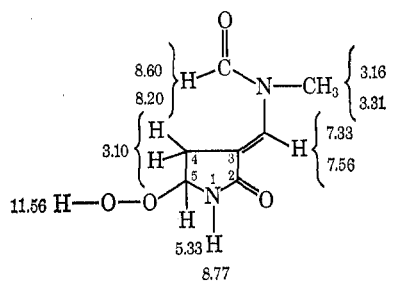
onance of the region at 3.10 ppm, at which the 4-methylene protons absorb, shows that these protons are coupled both to the methine proton at C-5 and to the vinyl proton.



A

The absorptions caused by the methyl (or benzyl), vinyl, and formyl protons of **2a**, **2b**, **5**, and **6** are split each into two components of unequal intensity which is caused by restricted rotation about the carbon–nitrogen bond of the formamido group and is characteristic of unsymmetrical N,N-disubstituted formamides.[11] Models indicate that the methyl group would prefer to be *trans* to the carbonyl group. The predominant rotamer in tertiary formamides is the one in which the bulkier group on nitrogen is *trans* to the carbonyl group.[11]

The melting points of **2a** and **2b** are sharp which indicates the probable absence of a mixture of geometrical isomers, and samples behave homogeneously on thin layer chromatography on silica gel with several solvents. The observation of a high absorptivity in the ultraviolet spectrum of **2a** and **2b**, favors a *trans* orien-

(9) We are indebted to Dr. Kurt L. Loening, Director of Nomenclature, Chemical Abstracts Service, American Chemical Society, for assistance in naming **2** and its derivatives.

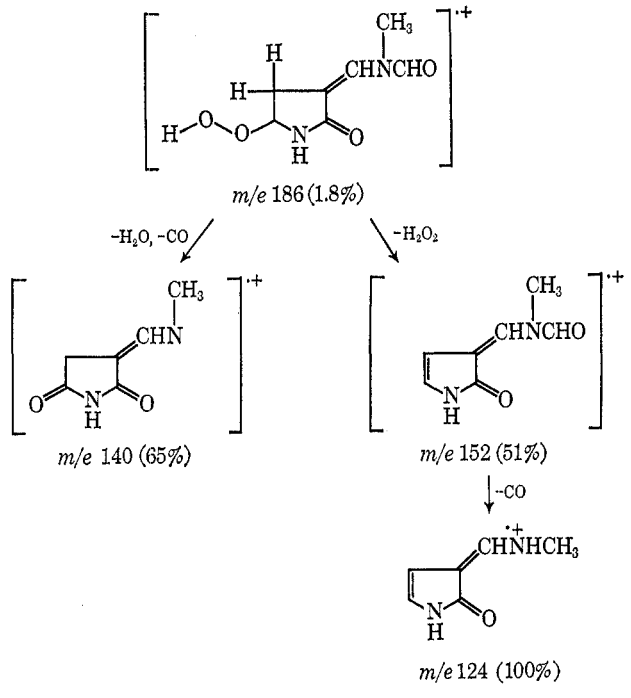
(10) These infrared absorptions may be the result of more complex vibrations than the simple stretching vibrations.

(11) J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Vol. 1, Pergamon Press, New York, N. Y., 1965, p 553.

tation of amido groups.[12] Accordingly, only one double-bond isomer is believed to be formed, probably of the configuration shown in structure A.

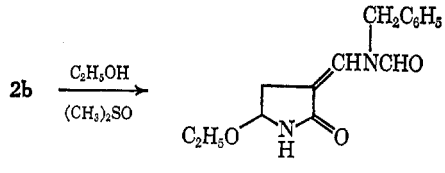
A rationalization of the major peaks of the mass spectrum of hydroperoxide **2a** is given in Scheme III.[13]

SCHEME III



The ion fragment *m/e* 124 also appears in the mass spectra of alcohol **3** ($M^+ - H_2O - CO$) and of diene **4** ($M^+ - CO$) which indicates the similarity of structure of these three compounds. The loss of carbon monoxide with rearrangement of the formyl proton is involved in the formation of the base peak in the mass spectra of each of the compounds containing chromophore **10**.[14] Similar fragmentations are observed for **2b**.

When **2b** is heated on a steam bath with ethanol and dimethyl sulfoxide, an ethyl ether is formed.



Conversion of Hydroperoxide 2a to N-Methylpyrrolidinone 6.—The hydroperoxy group of **2a** (or **2b**) is reduced to an hydroxyl group by 1 mol of hydrogen. Use of palladium on charcoal instead of platinum oxide results also in reduction of the carbon–carbon double bond to yield saturated alcohols. Ultraviolet absorption of alcohol **3** at 264 mμ (ε 21,200) and infrared absorptions at 1706, 1672, and 1620 indicate that chromophore **10** is still present.

The hydroxyl group of **3** is in the 5 rather than the 4 position because the chemical shift of the methine proton (δ 5.13) is at lower field than is typical for an unsubstituted secondary alcohol and this chemical shift is in good agreement with chemical shifts tentatively reported for the methylene protons of N-hydroxymethyl-N-methylformamide (δ 5.09) and N-hydroxymethyl-N-benzylformamide (δ 5.05).[15] Irradiation of the vinyl proton causes the absorption of the methylene group at C-4 to simplify but has no effect on the methine absorption, consistent with the hydroxyl group being at position 5.

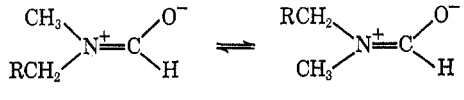
The mass spectrum of **3** shows a base peak for a fragment (*m/e* 124) corresponding to the loss of water and carbon monoxide from the molecular ion and an intense peak for a fragment (*m/e* 152) corresponding to the loss of water only from the molecular ion. Similar behavior occurs with the alcohol derived from **2b**.

Dehydration to the diene **4** occurs when alcohol **3** is treated with acetic anhydride in dry pyridine. Infrared nmr, and ultraviolet spectra show the presence of chromophore **10** and the pyrrolidinone ring. Two maxima, 263 mμ (ε 17,400) and 361 (7500), in the ultraviolet spectrum may be attributed to the cross-conjugated system in **4**.[16] The most abundant ion in the mass spectrum of **4** is at *m/e* 124 and is produced by loss of carbon monoxide from the parent ion.

Hydrogenation of diene **4** over palladium on charcoal gives completely reduced pyrrolidinone **5**. Selective hydrogenation of the carbon–carbon double bond in the ring occurs to give **4a** when platinum oxide was used as catalyst, the reaction being stopped after the uptake of 1 equiv of hydrogen. Treatment of saturated pyrrolidinone **5** with sodium hydride in dimethylformamide–benzene[17] yields the sodium salt which is methylated by treatment with methyl iodide to yield **6**.

The spectroscopic properties of **5** and **6** are similar. In the solid phase, absorption in the infrared spectrum of **5** occurs at 3200 (intermolecularly hydrogen-bonded N–H), 1705 (pyrrolidinone carbonyl), and 1660 cm^{-1} (formamide carbonyl) while in solution in carbon tetrachloride the corresponding absorptions are at 3445, 1713, and 1678 cm^{-1}.

The nmr absorption for the N-methyl protons of the formamido group of **5** and **6** appears as two lines of approximately equal intensity. Their separation is field and temperature dependent which indicates restricted rotation in the formamido group as observed in the other intermediates described above. The formyl proton was not affected by the rotational isomerism since its environment in the two rotamers is essentially the same. The absorption of the methylene protons [$-CH_2N(CH_3)CHO$] adjacent to the 3 position of the



(12) A *cis*-oriented model has a lower molar absorptivity: Sadtler Standard Ultraviolet Spectrum No. 5552, Sadtler Research Laboratories, Philadelphia, Pa., 1965.

(13) Intensities are given in terms of per cent of the base peak. Other structures for the ions may be written.

(14) Loss of carbon monoxide with rearrangement of the formyl proton is observed in the mass spectra of N-formyl-α-amino acid esters: K. Heyns and H.-F. Grützmacher, *Z. Naturforsch. B*, **16**, 293 (1961).

(15) J. P. Chupp and A. J. Speziale, *J. Org. Chem.*, **28**, 2592 (1963).

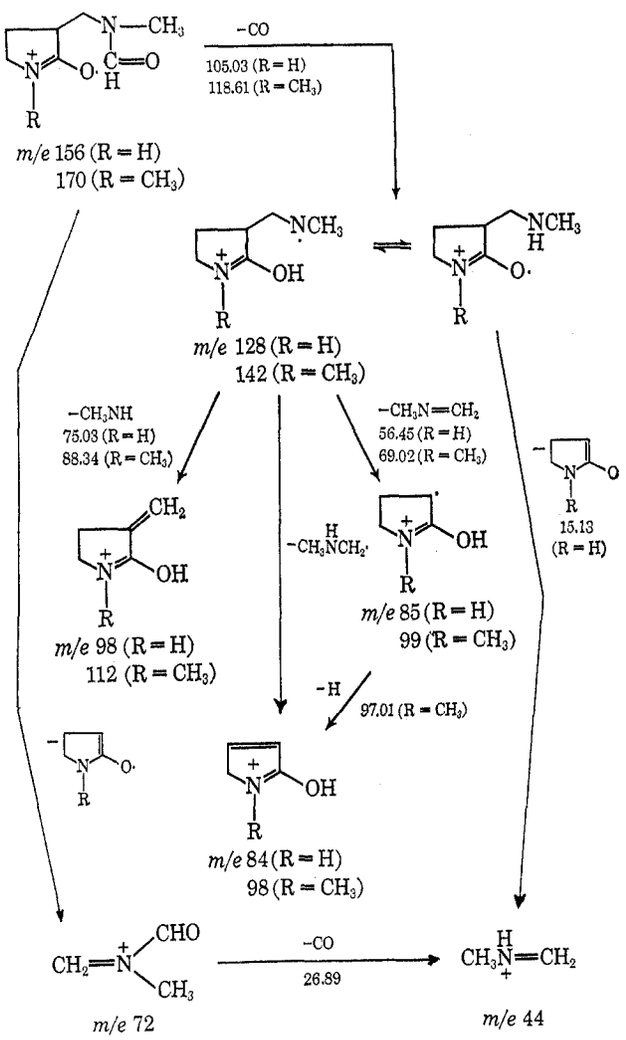
(16) 1-Alkyl-3-substituted 1,6-dihydropyridines which are cross conjugated show two maxima at longer wavelengths than observed for 1,4-dihydropyridine derivatives: K. Wallenfels and H. Schüly, *Justus Liebigs Ann. Chem.*, **621**, 106 (1959).

(17) The sodium salt is insoluble in dimethylformamide but addition of benzene results in dissolution of the salt. Without addition of benzene, no alkylated product is obtained with methyl iodide.

pyrrolidinone ring is complex and apparently comprises two sets of multiplets (each of which is the AB part of an ABX spectrum).

Use of the N-methyl group on the pyrrolidinone nitrogen in **6** as a label in mass spectrometry together with metastable ion transitions is helpful in interpretation of the mass spectra of **5** and **6** in terms of their structures. A rationalization of the important features of the mass spectra of **5** and **6** is outlined in Scheme IV.

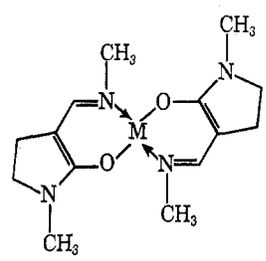
SCHEME IV



Other structures for the ions may be written in which charge is localized in the formamide group. Where metastable ion transitions were observed, the calculated *m/e* values are indicated in the scheme beside the arrows. Loss of carbon monoxide from the molecular ions of **5** and **6** is important but its loss from N,N-dimethylformamide is not,[18] possibly because there is no easy way to rearrange the formyl hydrogen in the latter.

Synthesis of 6 from 1-Methyl-2-pyrrolidinone.—Scheme II depicts the steps of the synthesis. The known enol, 3-hydroxymethylene-1-methyl-2-pyrrolidinone[19] (**7**), is treated with excess methylamine in dry ethanol to yield the enaminoamide **8**. The ultraviolet spectrum of **8** disappears on addition of 1 drop of dilute acid. Enaminoamide **8** is formed as a mixture of *cis* and *trans* isomers. The *cis* form appears to predominate in dilute solution while the *trans* form predominates in the solid phase.[20]

The enaminoamide forms an intense blue color with Fe^{III} ions and a green complex with Cu^{II} ions. Formation of a stable complex such as **12** may explain why the olefinic double bond could not be hydrogenated over platinum oxide or over 5% palladium on charcoal at atmospheric pressure.



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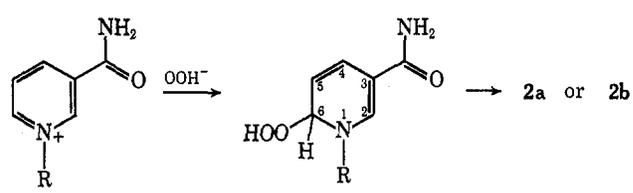
Formylation of **8** by formic–acetic anhydride gives **9**, whose spectra are similar to those of the partially hydrogenated product **4a** obtained from diene **4**.

The most abundant ion in the mass spectrum of **9** and enaminoamide **8** is at *m/e* 140. The fragmentation patterns of these compounds are very similar. These similarities may be attributed to the formation of an abundant ion of identical structure from either **9** or **8**.

Hydrogenation of **9** over palladium on charcoal gives 1-methylpyrrolidinone **6** whose properties were identical with those of the pyrrolidinone obtained by degradation of the product (**2a**) from 1-methyl-3-carbamoylpyridinium chloride and alkaline hydrogen peroxide.

Mechanistic Considerations.—In the reaction of the pyridinium salt with hydrogen peroxide in sodium bicarbonate, the pH of the solution decreases with time as carbon dioxide is evolved. This may be interpreted as a decrease in the concentration of hydroperoxide anion resulting from its addition to the pyridinium ring. Although addition can occur at either the 2, 4, or 6 positions, the structure of the product indicates that it probably arises from attack at the 6 position.[21] Enzymic oxidation of nicotinic acid occurs *via* oxidation of the 6 position.[22]



A possible mechanism which accounts for the formation of product **2** is given in Scheme V. An analogy is the reaction of 5,6-diphenyl-2,3-dihydropyrazine with

(18) Catalog of Mass Spectral Data, American Petroleum Institute Research Project 44, National Bureau of Standards, Serial No. 113, 1951. The base peak is caused by loss of HCO.

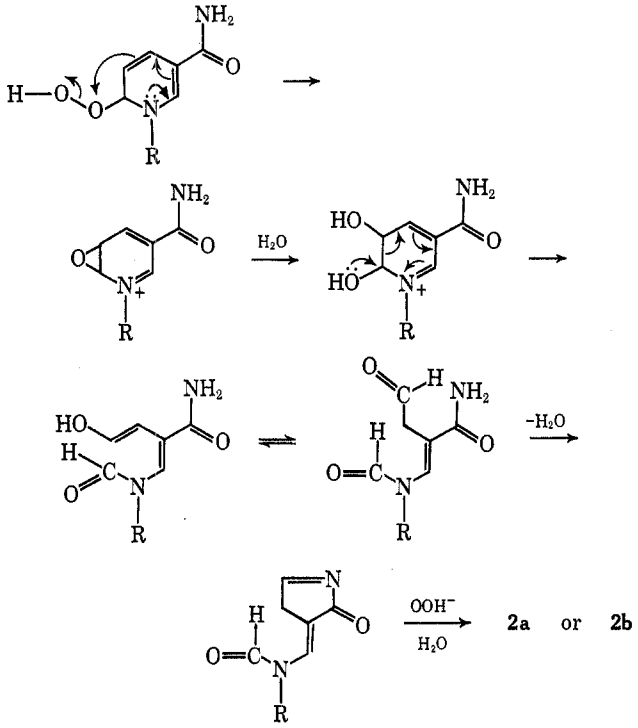
(19) K. H. Büchel and F. Korte, *Chem. Ber.*, **95**, 2465 (1962).

(20) *cis* and *trans* isomerism in similar compounds has been investigated by infrared and nmr: J. Dabrowski and U. Dabrowski, *ibid.*, **101**, 2365 (1968); G. O. Dudek and G. P. Volpp, *J. Amer. Chem. Soc.*, **85**, 2697 (1963).

(21) No product is formed when distilled, deionized water is used as solvent. Metal ions present in the tap water may catalyze the decomposition of the hydroperoxide adduct or the further oxidation of the ring. See A. R. Doumaux, Jr., J. E. McKeon, and D. J. Trecker, *ibid.*, **91**, 3992 (1969), for recent examples of metal-ion-catalyzed oxidations.

(22) D. A. Hughes, *Biochem. J.*, **60**, 303 (1955).

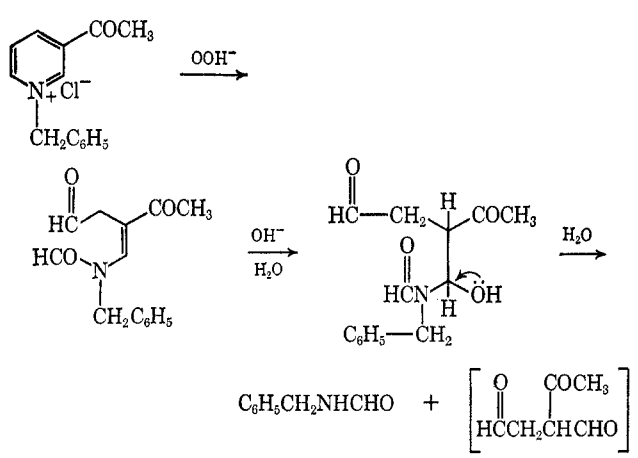
SCHEME V



methanolic hydrogen peroxide which also results in a ring opening and contraction to a five-membered ring.[23]

Treatment of 1-Benzyl-3-acetylpyridinium Chloride and 1-Benzyl-3-bromopyridinium Chloride with Alkaline Hydrogen Peroxide.—N-Benzylformamide was isolated in 6% yield on treatment of 1-benzyl-3-acetylpyridinium chloride with hydrogen peroxide and aqueous sodium bicarbonate, and N-benzyl-2,2-dibromoacetamide was obtained in 2% yield from 1-benzyl-3-bromopyridinium chloride. Traces of other oily products were obtained but were not identified.

N-Benzylformamide may be considered as arising from an intermediate analogous to that proposed in the decomposition of 1-methyl-3-carbamoylpyridinium chloride. Formation of N-benzyl-2,2-dibromoacetamide from 1-benzyl-3-bromopyridinium chloride may occur *via* bromination of N-benzyl-2-bromoacetamide[24] by molecular bromine produced by oxidation of bromide



ion formed by a displacement or elimination reaction from the pyridinium salt.

Experimental Section

Melting points were obtained on a Fisher-Johns melting point apparatus and are corrected unless otherwise indicated. Microanalyses were performed at Galbraith Laboratories, Knoxville, Tenn., or at Alfred Bernhardt Microanalytisches Laboratorium in Max-Planck-Institut für Kohlenforschung, Mülheim, West Germany. Molecular weights were determined by vapor pressure osmometry or by mass spectrometry. Infrared spectra were obtained on either a Perkin-Elmer Model 521 grating spectrophotometer or a Perkin-Elmer Model 137 sodium chloride spectrophotometer. The infrared absorptions are in cm^{-1} and the relative intensities are given as weak (w), medium (m), and strong (s). Ultraviolet spectra were obtained on a Perkin-Elmer Model 202 ultraviolet-visible spectrophotometer. The absorptions are reported in $m\mu$ and their intensity (ϵ) in liter/mole centimeter. Proton nuclear magnetic resonance (nmr) spectra were obtained on either a Jeolco Model 4H-100 or a Varian Model A-60 nuclear magnetic resonance spectrometer. Chemical shifts are reported as δ values using tetramethylsilane or sodium 2,2-dimethyl-2-silapentane-5-sulfonate as an internal standard. The absorption position of a complex multiplet is reported as the center of the absorption. Abbreviations used in reporting nmr data in tables are b, broad; m, complex multiplet; s, singlet; d, doublet; t, triplet. Mass spectra were obtained on a Perkin-Elmer Hitachi Model RMU-6E single-focusing spectrometer. Only those peaks of mass greater than 29 and which are 5% or more of the base peak or which have special significance are reported. Thin layer chromatography (tlc) was performed according to standard methods[25] by use of either Eastman Chromatogram Sheet 6060 (silica gel) or 6063 (alumina) or apparatus from Brinkman Instruments, Inc., Westbury, N. Y., and Merck silica gel HF_{254}.

Reaction of 1-Methyl-3-carbamoylpyridinium Chloride with Hydrogen Peroxide and Sodium Bicarbonate. N-[(5-Hydroperoxy-2-oxo-3-pyrrolidinylidene)methyl]-N-methylformamide (2a).—Treatment of 1-methyl-3-carbamoylpyridinium chloride[26] (17.3 g, 0.100 mol) with 30% hydrogen peroxide (30.9 ml, 0.300 mol) (Baker and Adamson) and sodium bicarbonate (8.41 g, 0.100 mol) (Baker and Adamson, anhydrous) in tap water (110 ml) at 0–5° gave a pale yellow solution which had a pH of 8.0. After 8 days at 0–5°, the pH of the yellow solution was 5.0 and a white solid had begun to precipitate. After 3 months, the mixture was filtered and the solid was washed thoroughly with cold water and dried overnight under vacuum at room temperature to yield a granular, white solid (1.49 g, 8.0%). Reaction times of 1 month gave slightly lower yields. Two recrystallizations from 95% ethanol gave a white solid, mp 161–162° dec. Use of a tenfold excess of either 30 or 50% hydrogen peroxide did not affect the yield.

Anal. Calcd for $C_7H_{10}N_2O_4$: C, 45.16; H, 5.41; N, 15.05; mol wt, 186.2. Found: C, 45.20; H, 5.34; N, 14.92; mol wt, 190 (ethanol).

The compound was soluble in dilute sodium hydroxide solution and in triethylamine, gave a positive test for peroxide with potassium iodide–starch paper, decolorized bromine water and potassium permanganate solution, and gave a purple color with ferric chloride solution after treatment with a basic solution of hydroxylamine. Thin layer chromatography (Merck, silica gel HF_{254}) gave only one spot (solvent, R_f): chloroform, 0.00; 1:1 chloroform–ethanol, 0.31; ethanol 0.52; 95% ethanol, 0.65; water, 0.73; pyridine, 0.71. After the plate was developed and visualized in one direction, it was rotated 90° and developed again. Only a single spot was observed.

The following spectral properties were observed: uv max (95% ethanol) 264 $m\mu$ (ϵ 17,600); ir (KBr) 3400 (m), 3290 (s), 3240 (m), 3140 (m), 2940 (w), 2790 (w), 1717 (s), 1678 (s), 1635 (s), 1438 (m), 1430 (m), 1419 (m), 1395 (m), 1338 (m), 1298 (m), 1240 (s), 1213 (m), 1189 (m), 1107 (m), 1080 (s), 1068 (s), 1032 (m), 980 (m), 945 (w), 872 (m), 841 (m), 822 (w), 768 (m), 747 (m), 732 (m), 677 (m), 655 (m), 640 (m), 583 (m),

(23) H. I. X. Mager and W. Berends, *Recl. Trav. Chim. Pays-Bas*, **84**, 314 (1965).

(24) A speculative mechanism involving a 2-pyridone can be written for the formation of N-benzyl-2-bromoacetamide.

(25) J. Bobbitt, "Thin-Layer Chromatography," Reinhold Publishing Corp., New York, N. Y., 1963.

(26) P. Karrer, G. Schwarzenback, F. Benz, and U. Solmssen, *Helv. Chim. Acta*, **19**, 826 (1936).

and 512 (m) cm^{-1}; nmr (100 MHz, dimethyl sulfoxide-d_6) δ 11.56[27] (s, 0.93), 8.77[27] (broad, 1.0), 8.60 (s, 0.74), 8.20 (s, 0.26), 7.56 (t, 0.22), 7.33 (t, 0.78), 5.33 (m, 0.96), 3.10 (m), 3.31 (s), 3.16 (s, 4.9, combined with area of peaks at δ 3.10 and 3.31); nmr (100 MHz, pyridine-d_5) δ 13.7 (broad, 0.95), 10.2 (broad, 0.95), 8.67 (s, 0.87), 8.21 (s, 0.15), 8.36 (t, 0.23), 7.72 (t, 0.79), 5.83 (m, 1.00), 3.31 (m, 2.10), 3.09 (s, 2.94); mass spectrum (70 eV, direct inlet, ambient temperature) *m/e* (relative intensity) 186 (1.8), 170 (0.4), 169 (1.6), 168 (12.5), 158 (3.1), 153 (6.2), 152 (50.7), 142 (1.6), 141 (6.4), 140 (64.8), 139 (14.4), 126 (3.2), 125 (17.9), 124 (100), 123 (11.5), 112 (5.8), 111 (8.3), 109 (5.3), 99 (2.2), 98 (8.7), 97 (27.4), 96 (17.0), 95 (25.2), 94 (23.7), 93 (4.1), 84 (7.8), 83 (19.8), 82 (17.5), 81 (41.3), 80 (19.9), 70 (5.0), 69 (41.9), 68 (35.1), 67 (43.0), 66 (16.5), 59 (8.2), 58 (5.0), 57 (6.1), 56 (6.0), 55 (33.3), 54 (17.4), 53 (12.7), 52 (12.5), 51 (5.5), 46 (5.6), 45 (8.0), 44 (9.1), 43 (18.1), 42 (22.9), 41 (36.9), 40 (11.3), 39 (41.7), 38 (12.4), 36 (7.2), 34 (13.1), 33 (1.6), 32 (2.0), 31 (13.4), 30 (28.7).

N-Benzyl-N-[(5-hydroperoxy-2-oxo-3-pyrrolidinylidene)methyl]formamide (2b).—Treatment of 1-benzyl-3-carbamoylpyridinium chloride (9.96 g, 40.0 mmol) with 30% hydrogen peroxide (12.1 ml, 119 mmol, Baker and Adamson) and sodium bicarbonate (3.36 g, 40.0 mmol) (Baker and Adamson, anhydrous) in tap water (36 ml) gave a clear yellow solution, pH 8.5. The reaction mixture was refrigerated at 4° and an orange oil slowly separated on the bottom and sides of the flask. The pH of the solution decreased to 5. After 6 days, a small amount of white solid began to precipitate from the solution (pH 4.5). The oil and the precipitate were removed and the solution was returned to the refrigerator. The white solid continued to form and after 16 days it was removed by filtration and dried for 24 hr under vacuum at room temperature to give 0.40 g of solid, mp 133–140° cor. Addition of cold 95% ethanol to the oil and solid obtained by filtration caused the oil to dissolve, and an additional 0.24 g of crude white solid was obtained. The total yield of crude product was 6.1%. Three recrystallizations from absolute ethanol gave a white solid, mp 142.5–145° dec with evolution of gas.

When the benzylpyridinium salt was treated with a tenfold excess of 30% hydrogen peroxide, the reaction occurred without the formation of orange oil. After 6 days, a white solid began to form and the pH of the solution had changed from 8.5 to 5.0. Work-up gave relatively pure solid (7.3%) which was identical with that obtained above.

Anal. Calcd for $C_{13}H_{14}N_2O_4$: C, 59.54; H, 5.38; N, 10.68; mol wt, 262. Found: C, 59.63; H, 5.46; N, 10.63; mol wt, 266 (ethanol), 237 (tetrahydrofuran).

The following spectral properties were observed: uv max (95% ethanol) 264 mμ (ϵ 18,500); ir (KBr) 3400 (m, shoulder), 3240 (s), 3065 (w), 3035 (w), 2937 (w), 2905 (w), 1720 (s), 1688 (s), 1635 (s), 1498 (m), 1452 (m), 1404 (m), 1318 (m), 1265 (s), 1210 (m), 1159 (s), 1090 (m), 1077 (m), 1028 (w), 974 (m), 911 (m), 839 (m), 775 (w), 743 (w), 716 (m), 693 (w), 677 (w), 582 (w), 521 (w), and 462 (w) cm^{-1}; mass spectrum (70 eV, direct inlet, 150°) *m/e* (relative intensity) 262 (0.0), 244 (6.2), 229 (4.1), 228 (10.3), 217 (15.5), 216 (92.8), 215 (50.5), 201 (22.7), 200 (100), 199 (14.4), 171 (12.4), 156 (12.4), 145 (18.1), 144 (35.0), 143 (18.6), 142 (11.3), 135 (61.9), 134 (39.6), 130 (10.3), 128 (10.7), 118 (10.3), 117 (16.5), 116 (12.0), 115 (19.8), 109 (14.4), 107 (13.4), 106 (59.8), 105 (16.1), 104 (25.4), 95 (11.3), 94 (11.3), 93 (10.3), 92 (72.5), 91 (3210), 90 (24.7), 89 (37.1), 83 (10.9), 82 (24.7), 81 (19.6), 80 (10.3), 79 (37.1), 78 (22.7), 77 (43.3), 73 (11.3), 69 (15.5), 68 (14.4), 67 (20.6), 66 (21.6), 65 (177), 64 (18.6), 63 (47.4), 62 (12.4), 57 (14.4), 55 (35.0), 54 (37.1), 53 (28.9), 52 (41.2), 51 (69.1), 50 (30.9), 46 (14.4), 45 (19.0), 44 (38.1), 43 (20.6), 42 (14.4), 41 (60.2), 40 (22.7), 39 (139), 38 (27.2), 32 (4.1), 31 (10.3), 30 (25.8); nmr (100 MHz, dimethyl sulfoxide-d_6) δ 11.54[27] (s, 0.86), 8.85 (s), 8.46 (s), 8.78 (s, 2.00, combined with area of absorption at δ 8.85 and 8.46), 7.66 (t), 7.47 (t), 7.25 (m, 5.93, combined with area of absorption at δ 7.66, 7.47), 5.22 (m, 0.92), 4.96 (s), 4.91 (s, 2.16, combined with absorption at δ 4.96), 2.75 (m, 2.14); nmr (100 MHz, pyridine-d_5) δ 13.0 (broad), 9.01 (s, 0.83), 8.54 (s, 0.17), 10.2 (s, 0.96), 8.49 (t, 0.16), 7.97 (t, 0.86), 7.74 (s, 5.04), 5.67 (m, 1.00), 5.03 (quartet, 1.92), 3.09 (m, 2.05); nmr (60 MHz, acetic acid-d_4) δ 11.4[28] (s), 8.82 (s), 8.50 (s), 8.45 (t), 7.67 (t), 7.28 (s), 5.43 (m), 4.98 (s), 2.82 (m).

(27) Exchanges upon addition of deuterium oxide.

(28) Time-averaged absorption due to rapid chemical exchange with the solvent.

Catalytic Hydrogenation of N-[(5-Hydroperoxy-2-oxo-3-pyrrolidinylidene)methyl]-N-Methylformamide (2a). (a) Over Platinum Oxide. Preparation of N-[(5-Hydroxy-2-oxo-3-pyrrolidinylidene)methyl]-N-methylformamide (3).—The hydroperoxide **2a** (0.370 g, 2.00 mmol) in 175 ml of absolute ethanol was hydrogenated over platinum oxide catalyst (0.0110 g) at ambient pressure and temperature. Hydrogen uptake was rapid and complete in less than 90 min. A total of 2.2 mmol corresponding to 1.1 equiv of hydrogen was absorbed.

The catalyst was removed by filtration and the solvent was flash evaporated to yield a white solid, mp 180–200° dec. Recrystallization from absolute ethanol, filtration, and overnight drying at room temperature gave white crystals (0.260 g, 78%). A second recrystallization gave a sample: mp 200–205° dec (uncor) (turns slightly yellow above 150°); uv max (95% ethanol) λ_{max} 264 mμ (ϵ 21,200); ir (KBr disk) 3425 (OH), 3275 (OH), 3173 (NH), 3075 (NH), 1706 (HC=O), 1672 (pyrrolidone C=O), 1620 (C=C), 1451 (m) cm^{-1}; mass spectrum (70 eV, direct inlet, 100°) *m/e* (relative intensity) 152 (57.4), 142 (6.9), 141 (18.5), 140 (19.9), 124 (100); nmr (100 MHz, dimethyl sulfoxide-d_6), 8.59 (s, 0.64), 8.18 (s, 0.32), 8.38[27] (b, 1.00), 7.55 (t, 0.29), 7.31 (t, 0.77), 5.86 (d, 0.93), 5.13 (m, 0.99), 3.28 (s), 3.13 (s), 3.06 (m, 5.09, combined with area of absorption at δ 3.28 and 3.13); nmr (60 MHz, D_2O) 8.55 (s, 0.73), 8.22 (s, 0.34), 7.65 (t, 0.34), 7.36 (t, 0.73), 5.45 (four-line multiplet, 0.97), 3.68–2.80 (m, 5.13).

Anal. Calcd for $C_7H_{10}N_2O_3$: C, 49.41; H, 5.92; N, 16.46. Found: C, 49.45; H, 6.03; N, 16.27.

(b) Over 5% Palladium on Charcoal. N-[(5-Hydroxy-2-oxo-3-pyrrolidinyl)methyl]-N-Methylformamide.—The hydroperoxide (0.931 g, 5.00 mmol) in 425 ml of absolute ethanol was hydrogenated over 5% palladium on powdered charcoal (0.186 g, 20% of starting material by weight) at atmospheric pressure and room temperature. Hydrogen uptake was very fast for 10 min, slower but constant to 90 min, and complete after 110 min. A total of 8.6 mmol corresponding to 1.7 equiv of hydrogen was taken up (86%). The catalyst was removed by filtration and the solvent was flash evaporated to yield a colorless oil which solidified on standing. Recrystallization from ethanol–ether, filtration, and vacuum drying at room temperature gave 0.690 g (74%) of white crystals: mp 142–143° (uncor); ir (KBr) 3400 (m), (broad), 3200 (s), 2800 (w), 2725 (w), 1684 (s), 1647 (s), 1454 (m) cm^{-1}; mass spectrum (70 eV, direct inlet, ambient temperature) *m/e* (relative intensity) 172 (1.3), 154 (9.4), 144 (6.4), 126 (38.5), 84 (23.2), 72 (100), 71 (4.3); nmr (60 MHz, 4:1 dimethyl sulfoxide-d_6–chloroform-*d*) δ 8.21[27] (b, 1.92, combined with area of absorption at δ 8.06), 8.06 (s), 5.75 (m, 0.97), 5.16 (m, 1.24), 3.50 (m, 1.94), 2.95 (s), 2.80 (s), 2.9 to 1.51 (m, 6.06, combined with area of absorption at δ 2.95, 2.80).

Anal. Calcd for $C_7H_{12}N_2O_3$: C, 48.83; H, 7.02; N, 16.27. Found: C, 49.01; H, 7.06; N, 16.09.

N-Benzyl-N-[(5-Hydroxy-2-oxo-3-pyrrolidinylidene)methyl]-formamide.—A solution of the hydroperoxide **2b** (0.393 g, 15.0 mmol) in 85 ml of absolute ethanol was hydrogenated over platinum oxide (0.0188 g) at atmospheric pressure and room temperature. The catalyst was removed by filtration and the solvent was evaporated to give a solid. Recrystallization from 25 ml of absolute ethanol gave 0.283 g (77%) of white solid. A second recrystallization from ethanol gave a sample: mp 168–170° dec (turns slightly yellow above 155°); uv max (ethanol) 263 mμ (ϵ 18,500); ir (KBr) 3475 (OH), 3330 (OH), 3185 (NH), 3050 (NH), 3023 (w), 1726 (HC=O), 1685 (pyrrolidone C=O), 1644 (C=C) cm^{-1}; nmr (60 MHz, dimethyl sulfoxide-d_6) δ 8.86 (s, 0.87), 8.45 (s, 0.16), 8.37 (broad, 0.85), 7.67 (t), 7.45 (t), 7.27 (m, 6.4, integrated with absorption at δ 7.67, 7.45), 5.78 (d, 0.97), 5.04 (m), 4.89 (s, 3.03, integrated with absorption at δ 5.04), 2.70 (m, 1.78); nmr (pyridine-d_5) δ 8.95 (s, 0.86), 8.66 (s, 0.19), 9.40 (broad, 0.93), 8.35 (t, 0.18), 7.85 (t, 0.88), 7.23 (s, 5.14), 5.48 (m, 1.02), 4.99 (s, 1.87), 3.00 (m, 1.91); mass spectrum (70 eV, direct inlet, 100°) *m/e* (relative intensity) 246 (2.5), 228 (13.8), 218 (10.3), 200 (100), 91 (96.2), 65 (56.0), 39 (25.3).

Anal. Calcd for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.22; H, 5.84; N, 11.35.

N-Benzyl-N-[(5-hydroxy-2-oxo-3-pyrrolidinyl)methyl]formamide.—A solution of hydroperoxide **2b** (0.393 g, 1.50 mmol) in 175 ml of absolute ethanol was added to a slurry of prereduced 5% palladium on powdered charcoal (0.0786 g) in 10 ml of absolute ethanol. The mixture was hydrogenated at atmospheric

pressure and room temperature. Hydrogen uptake was very rapid for 15 min and then slow for 6 hr. A total of 1.9 equiv of hydrogen was absorbed. The catalyst was removed by filtration and the filtrate flash evaporated to yield a pale yellow oil which did not crystallize on vacuum drying or on attempted crystallization from ethanol–ether or chloroform solution: ir (KBr) 3420 (s, shoulder), 3320 (s, b), 3070 (w, shoulder), 2790 (w), 1705 (s), 1665 (s), 1440 (m) cm^{-1}; ir (chloroform solution), 3420 (m), 3350 (m), 1705 (s), and 1660 (s) cm^{-1}; nmr (60 MHz, chloroform-*d*), δ 8.28 (s), 8.22 (s, 0.74, combined with absorption at δ 8.28), 7.67 (broad, 0.97), 7.3 (broad), 7.29 (s, 6.01, integrated with the absorption at δ 7.3), 4.52 (s), 4.47 (s, 2.08, integrated with absorption at δ 4.52), 3.51 (m, 2.11), 2.9–1.5 (two multiplets, 2.86).

N-Methyl-N-[(5-oxo-2-pyrrolin-4-ylidene)methyl]formamide (4).—Acetic anhydride (1.9 ml, 20.0 mmol) was added to a slurry of the unsaturated alcohol (0.340 g, 2.00 mmol) in 12.0 ml of anhydrous pyridine (distilled from molecular sieves 4A powder) in a 25-ml erlenmeyer flask. The flask was stoppered and the mixture was stirred magnetically at room temperature. The slurry became red upon mixing and very dark after several hours. Reaction progress was followed by tlc on Eastman silica gel strips (sheet 6060). After 16 hr, the slurry was cooled to −20° and filtered to give a dark solid which was washed with ethanol and vacuum dried to give 0.155 g of yellow solid. The filtrate was distilled to dryness (*ca.* 1 mm) at room temperature to give a black residue. Addition of a few milliliters of water and filtration gave an additional 16 mg of yellow solid. The total yield of dried product was 0.171 g (56%). Another reaction gave an 80% yield. Two recrystallizations from 95% ethanol gave a sample: mp 227–230° dec (uncor); uv max (95% ethanol) 263 mμ (ϵ 17,400), 361 (7500), (methanolic HCl) 266, 327 mμ; ir (KBr) 3120 (NH), 3060 (NH), 1700 (HC=O), 1673 (pyrrolidone C=O), 1582 (C=C), 1545 (C=C), cm^{-1}; mass spectrum (70 eV, direct inlet, 150°) *m/e* (relative intensity) 152 (21.9), 124 (100), 94 (18.7), 81 (45.3); nmr (100 MHz, dimethyl sulfoxide-d_6) δ 9.55[27] (b, 0.94), 8.77 (s, 0.76), 8.33 (s, 0.10), 7.69 (d, 0.07), 7.52 (d, 0.85), 6.69 (m, 1.10), 5.99 (d, 1.01), 3.35 (s), 3.23 (s).

Anal. Calcd for $C_7H_8N_2O_2$: C, 55.26; H, 5.30; N, 18.41. Found: C, 55.30; H, 5.25; N, 18.48.

N-Methyl-N-[(2-oxo-3-pyrrolidinyl)methyl]formamide (5).—A slurry of the diene **4** (0.304 g, 2.00 mmol) in 130 ml of 95% ethanol was hydrogenated over 5% palladium on powdered charcoal (0.0761 g) at atmospheric pressure and room temperature. Hydrogen uptake was very fast and complete in 30 min. A total of 4.01 mmol corresponding to 2.00 equiv of hydrogen was taken up. A plot of volume of hydrogen *vs.* time for the reaction showed no clean break in the resulting curve. The catalyst was removed by filtration and the solvent was flash evaporated to a colorless oil which turned yellow on standing. The oil was taken up in chloroform, applied to a 22 × 30 mm column of Florisil, and eluted with methanol. The methanol was removed by flash evaporation, and the resulting oil partially solidified on standing and was recrystallized from ethanol–ether to give 0.206 g (66%) of yellow, granular solid, mp 73–75°. Two further recrystallizations gave a sample: mp 78.5–80°; ir (KBr) 3200 (NH), 3075 (NH), 1705 (pyrrolidone C=O), 1660 (HC=O), 1450 (NH) cm^{-1}; mass spectrum (20 eV, direct inlet, 120°) *m/e* (relative intensity) 156 (2.8), 141 (0.2), 129 (7.4), 128 (100), 127 (7.5), 126 (4.8), 113 (1.7), 105.0, 99 (4.3), 98 (18.4), 86 (4.1), 85 (74.9), 84 (19.1), 75.0, 72 (8.4), 56.4, 44 (52.6), 30 (1.8), 26.9, 20.0, 19.8, 15.1; nmr (100 MHz, chloroform-*d*) δ 8.08 (s), 8.07 (s, 1.00, integrated with absorption at δ 8.08), 7.25[27] (d, 0.86), 3.58 (m), 3.37 (m, 4.18, integrated with absorption at δ 3.58), 2.99 (s), 2.89 (s, 2.92, integrated with absorption at δ 2.99), 2.65 (m, 1.25), 2.05 (m, 1.82).

Anal. Calcd for $C_7H_{12}N_2O_2$: C, 53.83; H, 7.74; N, 17.94. Found: C, 54.01; H, 7.63; N, 17.87.

N-Methyl-N-[(2-oxo-3-pyrrolidinylidene)methyl]formamide (4a).—A slurry of diene **4** (0.228 g, 1.50 mmol) in 100 ml of 95% ethanol was hydrogenated over platinum oxide (0.228 g) at atmospheric pressure and room temperature. Hydrogen uptake was moderate but stopped abruptly after 15 min. Only 0.32 equiv of hydrogen had been taken up. Since all of the diene had dissolved, the catalyst was removed by filtration. A fresh portion of platinum oxide (0.045 g) was added and the hydrogenation resumed. In 25 min, an additional 0.65 equiv of hydrogen was taken up (97% of theory) and uptake stopped. The catalyst was removed by filtration and the filtrate was flash evaporated to give a white solid. The solid was recrystallized from absolute ethanol–ether (*ca.* 1:2) and vacuum dried at room temperature to give 0.098 g (43%) of tan solid. A second recrystallization from ethanol–ether with the aid of activated charcoal gave white needles: mp 173.5–175.5° dec; uv max (95% ethanol) 264 mμ (ϵ 20,700); nmr (100 MHz, dimethyl sulfoxide-d_6) δ 8.62 (s, 0.71), 8.21 (s, 0.24), 7.83 (broad, 0.94), 7.54 (t, 0.27), 7.28 (t, 0.80), 3.34 (m), 3.33 (s), 3.18 (s), 3.10 (m, 7.06, integrated with absorption at δ 3.34, 3.33, 3.18); mass spectrum (70 eV, direct inlet, ambient temperature) *m/e* (relative intensity) 154 (11.9), 126 (100), 97 (38.0), 69 (55.7), 68 (69.8), 42 (43.1); ir (KBr), 3170 (NH), 3085 (NH), 1708 (HC=O), 1695 (pyrrolidone C=O), 1630 (C=C), 1458 (NH) cm^{-1}.

Anal. Calcd for $C_7H_{10}N_2O_2$: C, 54.54; H, 6.54; N, 18.17. Found: C, 54.72; H, 6.52; N, 18.21.

N-Methyl-N-[(1-methyl-2-oxo-3-pyrrolidinyl)methyl]formamide (6).—Mineral oil was removed from sodium hydride (93 mg, 56.8% dispersion in mineral oil, 2.2 mmol) (Metal Hydrides, Inc.) by addition and decantation of three 2-ml portions of dry dimethylformamide (distilled from calcium hydride). The washed sodium hydride was transferred to a 25-ml, round-bottomed, three-necked flask (dried in an oven and cooled in an atmosphere of dry nitrogen) with the aid of 2 ml of dry dimethylformamide. The slurry was stirred under dry nitrogen at room temperature while a solution of N-methyl-N-[(2-oxo-3-pyrrolidinyl)methyl]formamide (**5**) in 3 ml of dry dimethylformamide was added dropwise through a serum cap over a 15-min period. Gas evolution was observed. Addition of 2 ml of dry benzene (distilled and stored over sodium) to the slurry caused all the solid material to dissolve, resulting in a yellow solution which was stirred at room temperature for 1.25 hr. Dropwise addition of methyl iodide (0.137 ml, 2.2 mmol) (Eastman) to the solution over a 2-min period caused the temperature of the reaction mixture to rise slightly. The flask and contents were cooled in a bath of cool water, a gelatinous precipitate formed, and the mixture was stirred for 2 hr longer at room temperature before an additional portion of methyl iodide (0.137 mmol, 2.2 mmol) was added. Stirring was continued overnight under a nitrogen atmosphere.

Water (1 ml) was added to the reaction mixture and the solid material dissolved. More water (3 ml) and benzene (2 ml) were added until layers formed. The benzene layer was removed and the solution was extracted with three 1-ml portions of benzene and five 1-ml portions of chloroform. The combined extracts were dried over 2 g of crushed Drierite, filtered, and concentrated by flash evaporation to *ca.* 10–15 ml. The remaining solvent (mainly dimethylformamide) was distilled above 0.5 mm with the aid of a warm water bath to give a light orange oil (**6**). Tlc of the oil on Eastman silica gel 6060 strips in methanol gave a single spot at R_f 0.66. An nmr spectrum of the oil revealed that the sample contained a small amount of stopcock grease (Apiezon L) impurity; ir (liquid between NaCl disks) 2915 (m), 2880 (m), 1680 (s), 1495 (m), 1430 (m), 1390 (s), 1295 (m), 1255 (m), 1225 (w), 1115 (w), 1090 (m), 1075 (m), 1008 (w), 950 (w), 795 (w), 728 (w), and 710 (w) cm^{-1}; ir (CCl_4 solution) 2920 (m), 2848 (m), 1684 (s), 1495 (w), 1429 (w), 1402 (m), 1381 (m), 1292 (m), 1255 (m), 1212 (w), and 1070 (m) cm^{-1}; nmr (chloroform-*d*, 60 MHz) δ 8.11 (s, 0.99), 3.46 (m, 4.20), 3.00 (s), 2.88 (s), 2.63 (m, 6.91, integrated with absorptions at δ 3.00 and 2.88), 2.00 (m, 1.90); mass spectrum (20 eV, indirect inlet, *ca.* 100°) *m/e* (relative intensity) 172 (1.0), 171 (6.2), 170 (47.6), 155 (0.5), 143 (5.1), 142 (60.4), 141.3, 141 (16.8), 140 (8.5), 127 (3.1), 118.6, 115.3, 113 (8.1), 112 (43.2), 111 (17.1), 110 (11.3), 99 (100), 98 (97.5), 97.0, 88.3, 84 (10.5), 72 (17.5), 70 (6.2), 69.0, 44 (47.8), 42 (4.4).

3-Hydroxymethylene-1-methyl-2-pyrrolidinone (7).—Formylation of 1-methyl-2-pyrrolidinone (Eastman) was done according to the procedure of Korte and Büchel.[19] Purified potassium[29] (41.0 g, 1.00 mol) under dry toluene (600 ml) (dried over calcium chloride and then fresh potassium) was powdered by vigorously shaking the heated mixture. After being cooled to room temperature, the slurry was poured into a 2-l., 3-necked, round-bottomed flask equipped with a mechanical stirrer, water condenser, and addition funnel. The toluene was pipetted off and replaced with 200 ml of dry ether (distilled from lithium aluminum hydride). The suspension was stirred and cooled in

(29) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," John Wiley & Sons, Inc., N. Y., 1967, p 905.

an ice bath as a mixture of 1-methyl-2-pyrrolidinone (114 g, 1.14 mol) (Eastman, practical) (distilled from calcium hydride) and ethyl formate (114 g, 1.50 mol) (dried over potassium carbonate and distilled from phosphorus pentoxide) in 100 ml of dry ether was added slowly (1.5 hr). During the addition, the reaction mixture turned red-brown and a salt precipitated. The ice bath was removed and the reaction mixture was stirred at room temperature. After 22 hr, the salt was filtered from the solution and stirred into 250 ml of 5 *M* hydrochloric acid (1.5 mol) with cooling. The acidified solution was filtered from inorganic salts and extracted with chloroform until the aqueous phase gave only a very slight enol reaction with ferric chloride (16 50-ml extractions). The chloroform extracts were dried overnight over Drierite and filtered; the chloroform was flash evaporated to give a yellow liquid. The concentrated extracts were fractionally distilled under reduced pressure. Chloroform was collected below room temperature (0.1 mm); a large amount of unreacted 1-methyl-2-pyrrolidinone was collected at 40–48° (0.1 mm); and a third constant boiling fraction was collected at 88° (0.1 mm). The third fraction distilled as a yellow oil which solidified on standing for a few minutes at room temperature. A large amount of charred material did not distil. The solid product was broken up and thoroughly washed with cold ether by suction filtration. Vacuum drying at room temperature for 4 hr gave 4.56 g (3.6%) of a yellow solid, mp 90–100°, and a small amount of the solid was recrystallized from acetone–petroleum ether (30–60°), mp 96–100° (lit.[19] mp 98°). The hydroxymethylene compound in water gave an intense green-blue color with 5% ferric chloride and a green color with cupric acetate. It had the following spectral properties: uv max (95% ethanol) 242 mμ (lit.[19] 241 mμ, log ε 4.17); ir (KBr) 2675 (broad, chelated OH), 1695 (C=O), 1635 (C=C) cm^{-1}; nmr (dimethyl sulfoxide-d_6, 60 MHz) δ 9.72 (s, OH or CHO), 7.13 (broad, OH or CHO), 3.33 (t, α-CH_2), 2.76 (s, CH_3), 2.55 (complex, β-CH_2 or methine proton), 3.7–1.9 (complex and broad, β-CH_2 or methine proton); mass spectrum (70 eV, indirect inlet) *m/e* (relative intensity) 127 (36.6), 126 (9.2), 99 (100), 98 (96.6).

1-Methyl-3-[(methylamino)methylene]-2-pyrrolidinone (8).—A solution of methylamine (18 ml, 0.40 mol) in 50 ml of cold, absolute ethanol was poured into a stirred solution of 3-hydroxymethylene-1-methyl-2-pyrrolidinone (**7**, 1.27 g, 0.010 mol) in 25 ml of absolute ethanol. The flask was protected by a drying tube and left at room temperature overnight. The solution was flash evaporated to a cream-colored solid which was taken up in hot methyl ethyl ketone and decolorized with activated charcoal. Addition of petroleum ether (bp 30–60°) to near the cloud point and refrigeration gave 0.926 g (66%) of light yellow solid: mp 134–138°; uv max (95% ethanol) 286 mμ (ε 26,000) (absorption completely disappears upon addition of a drop of dilute HCl); ir (KBr) 3263 (NH *trans*), 3155 (NH *cis*), 2912 (w), 2868 (w), 2846 (w), 2825 (w), 1674 (C=O), 1608 (C=C) cm^{-1}; ir (chloroform solution) 3420 (NH), 3340 (NH), 1690 (C=O), 1645 (C=C) cm^{-1}; nmr (chloroform-*d*, 60 MHz) δ 6.85[30a] (d, 0.73), 6.23[30a] (d, 0.15), 4.33[27] (b), 3.36 (t, 3.30, J = 7 Hz, integrated with absorption at δ 4.33), 2.86[30b] (m), 2.84 (s, 6.25, integrated with absorption at δ 2.86), 2.55 (t, 1.58, J = 7 Hz); mass spectrum (70 eV, indirect inlet, ambient temperature) *m/e* (relative intensity) 140 (100), 98 (40.8), 69 (53.0), 68 (64.3), 42 (46.5).

Anal. Calcd for $C_7H_{12}N_2O$: C, 59.98; H, 8.63; N, 19.98. Found: C, 60.04; H, 8.66; N, 19.86.

N-Methyl-N-[(1-methyl-2-oxo-3-pyrrolidinylidene)methyl]-formamide (9).—The formylation procedure described by Huffman was followed.[31] Acetic formic anhydride was prepared by heating acetic anhydride (0.378 ml, 4.00 mmol) and 98% formic acid (0.155 ml, 4.10 mmol) for 30 min at 56° (refluxing acetone bath) in a 5-ml round-bottomed flask equipped with a magnetic stir bar and a drying tube. The flask was transferred to a 26° water bath and 1-methyl-3-[(methylamino)methylene]-2-pyrrolidinone (**8**, 0.280 g, 2.00 mmol) was added to the stirred solution in small portions over a 5-min period. All of the solid dissolved. After 10 min, 2 ml of dry ether was added, resulting in precipitation of a cream-colored solid. The mixture was stirred at room temperature for 8.5 hr, filtered, washed with ether, and dried under vacuum for 1 hr at room temperature to give 0.186 g (55%) of tan solid, mp 150–152°. Refrigeration of the filtrate resulted in precipitation of an additional 37 mg of yellow solid bringing the yield to 66%. The product was recrystallized from absolute ethanol to give very fine white needles, mp 151.5–153°. A small sample was sublimed at 65–80° (0.25 mm) for microanalysis: uv max (95% ethanol) 267 mμ (ε 24,500); ir (KBr) 1702 (HC=O), 1671 (pyrrolidone C=O), 1624 (C=C) cm^{-1}; nmr (100 MHz, chloroform-*d*) δ 8.44 (s, 0.87), 8.07 (s, 0.10), 7.62 (t, 0.10), 7.27 (t, 0.92), 3.42 (m), 3.38 (s), 3.24 (s, 4.88, integrated with absorption at δ 3.42 and 3.38), 3.07 (m), 2.92 (s, 5.14, integrated with absorption at δ 3.07); mass spectrum (70 eV, direct inlet, ambient temperature) *m/e* (relative intensity) 168 (7.7), 140 (100), 116.7, 115.0, 109.0, 98 (23.2), 97 (21.2), 88.0, 69 (72.4), 68.6, 68 (69.2), 67.2, 67.0, 67 (9.7), 42 (64.6).

Anal. Calcd for $C_8H_{12}N_2O_2$: C, 57.13; H, 7.19; N, 16.66. Found: C, 56.85; H, 7.31; N, 16.50.

Synthesis of N-Methyl-N-[(1-methyl-2-oxo-3-pyrrolidinyl)-methyl]formamide (6).—A solution of N-methyl-N-[(1-methyl-2-oxo-3-pyrrolidinylidene)methyl]formamide (**9**, 0.16 g, 1.00 mmol) in 25 ml of absolute ethanol was hydrogenated over 5% palladium on powdered charcoal (0.0336 g) at atmospheric pressure and room temperature. Hydrogen uptake was smooth and stopped after 30 min when 0.86 equiv of hydrogen had been taken up. The catalyst was removed by filtration and the solvent was flash evaporated at 40° to give a colorless oil. The oil was taken up in ether, filtered, and refrigerated, but crystallization did not occur. Tlc of this solution on an Eastman silica gel 6060 prepared sheet in methanol gave a single spot at R_f 0.66 upon visualization with molecular iodine. The solvent was evaporated in a stream of nitrogen and the oil dried overnight under vacuum at room temperature: ir (liquid between disks, CCl_4 solution) identical with that of saturated methyl pyrrolidinone **6** obtained by methylation of **5**; nmr (60 MHz, chloroform-*d*) identical with that of saturated methyl pyrrolidinone **6** obtained by methylation of **5**; mass spectrum (20 eV, indirect inlet, 120°) *m/e* (relative intensity) 172 (0.5), 171 (4.7), 170 (11.7), 155 (0.2), 142 (37.2), 141.3, 141 (6.3), 140 (5.1), 127 (1.2), 118.6, 112 (22.4), 111 (7.1), 110 (4.9), 100 (6.4), 99 (100), 98 (43.0), 97.0, 88.3, 84, 72 (7.6), 69.0, 44 (29.6), 42 (2.0), 15 (0.1).

Samples of saturated methylpyrrolidinone **6** prepared by hydrogenation of **9** and by methylation of **5** were mixed together in chloroform solution. Tlc of this mixture on Eastman silica gel 6060 strips gave only one spot (solvent, R_f): ether, 0.05; chloroform, 0.12; methanol, 0.66 (development with iodine).

Reaction of N-Benzyl-N-[(5-Hydroperoxy-2-oxo-3-pyrrolidinylidene)methyl]formamide with Ethanol in Dimethyl Sulfoxide.—Absolute ethanol was added to a solution of hydroperoxide **2b** (75 mg, 0.3 mmol) in 0.5 ml of dimethyl sulfoxide-d_6. The solution was heated on a steam bath and concentrated by passing a stream of dry air over it. Alternate addition of ethanol and evaporation of solvent was repeated several times until crystals deposited from the concentrated solution. The mixture was refrigerated and filtered to give a yellow solid. Two recrystallizations from absolute ethanol gave white needles: mp 147–150° dec; uv max (ethanol) 264 mμ; ir (KBr) 3330 (NH), 3078 (NH), 1715 (HC=O), 1681 (pyrrolidone C=O), 1637 (C=C) cm^{-1}; mass spectrum (70 eV, direct inlet, 100°) *m/e* (relative intensity) 246 (2.2), 229 (2.3), 228 (10.5), 200 (100), 109 (3.9), 106 (3.1), 91 (184), 65 (18.0), 39 (5.3); nmr (100 MHz, chloroform-*d*) 8.69, (s, 0.80), 8.27 (s, 0.10), 8.07 (b, 0.75), 7.61 (t, 0.15), 7.45 (t, 0.90), 7.17 (m, 5.06), 4.90 (m, 3.11), 3.68 (m), 3.34 (m, 2.20, integrated with absorption at δ 3.68), 2.77 (m, 1.91), 1.30 (m), 1.19 (m, 3.00, integrated with absorption at δ 1.30).

Reaction of 1-Benzyl-3-acetylpyridinium Chloride with Hydrogen Peroxide and Sodium Bicarbonate.—Treatment of 1-benzyl-3-acetylpyridinium chloride (12.4 g, 50.0 mmol) with 30% hydrogen peroxide (15.2 ml, 148 mmol) and sodium bicarbonate (4.20 g, 50.0 mmol) in water (50 ml) gave an orange solution, pH 9. The pH was 6.0 after 12 hr at 0–5° and an orange oil had formed. After 9 days, the solution had a pH of 5.0. The solution was decanted from the oil which was rinsed several times with water, taken up in a minimum amount of chloroform, and applied to a 27 × 2 cm column of dry-packed Florisil (100–200 mesh). A bright yellow oil was eluted with 1:1 hexane–ether; a white solid was eluted with 1:2 hexane–ether; a pale yellow oil was eluted with ether. Elution with chloroform and finally

(30) (a) Collapses to a singlet upon addition of D_2O. (b) Changes multiplicity upon addition of D_2O.

(31) C. W. Huffman, *J. Org. Chem.*, **23**, 727 (1958).

with ethanol gave no other compounds, although dark-colored bands could be seen on the column.

The white solid was identified as N-benzylformamide, mp 59.5–60.5° (lit.[32] mp 60–61°). Its nmr spectrum was identical with that reported previously.[33]

Reaction of 1-Benzyl-3-bromopyridinium Chloride with Hydrogen Peroxide and Sodium Bicarbonate.—Treatment of 1-benzyl-3-bromopyridinium chloride (14.2 g, 50.0 mmol) with 30% hydrogen peroxide (15.2 ml, 148 mmol) and sodium bicarbonate (4.20 g, 50.0 mmol) in water (50 ml) yielded a yellow solution, pH 9.0. After 6 days at 0–5°, an oil had begun to form. The solution had a pH of 8.0 and effervescence was noted. The evolved gas was passed through a trap filled with saturated barium hydroxide solution. A white precipitate was formed immediately, indicating that the gas contained carbon dioxide. A control test with air was performed.

After 30 days the solution had a pH of 8.0 and was decanted from the yellow-orange oil that had formed. The oil was rinsed with water, taken up in 15 ml of chloroform (solution turned dark in color), and poured onto a 31 × 2 cm column of dry Florisil (100–200 mesh). Elution of the column with 2:1 hexane–ether gave a small amount of yellow oil which darkened on standing, a colorless fraction which was evaporated to give a white solid (2%), and a second yellow oil in very low yield. The white solid was identified as N-benzyl-2,2-dibromoacetamide. It was recrystallized several times from ethanol–water: mp 136.5–138° (uncor) and mmp (with an authentic sample[34]) 138–139° (uncor); ir (KBr disk) 3410 (w, broad), 3260 (m), 1648 (s) cm^{-1}; nmr (60 MHz, chloroform-*d*) δ 7.33 (C_6H_5, s, 5.09), 6.92 (NH, broad, 0.91), 5.86 ($CHBr_2$, s, 1.03), 4.46 (CH_2, d, 1.98, J_{CH-NH} = 6.0 Hz); mass spectrum (70 eV, indirect inlet, 25°) *m/e* (relative intensity) 227 (47.1), 225 (47.6), 146 (32.8), 104 (20.0), 103 (13.3), 91 (100.0).

Anal. Calcd for $C_9H_9NOBr_2$: C, 35.31; H, 2.95; N, 4.56; Br, 52.06; mol wt, 307. Found: C, 35.06, 35.25; H, 2.83, 2.99; N, 4.41, 4.66; N, 52.06; 51.86; mol wt, 313 (chloroform).

Registry No.—Hydrogen peroxide, 7722-84-1; 1-methyl-3-carbamoylpyridinium chloride, 1005-24-9; 1-benzyl-3-carbamoylpyridinium chloride, 5096-13-9; N-[(5-hydroxy-2-oxo-3-pyrrolidinyl)methyl]-N-methylformamide, 24744-90-9; N-benzyl-N-[(5-hydroxy-2-oxo-3-pyrrolidinylidene)methyl]formamide, 24744-91-0; N-benzyl-N-[(5-hydroxy-2-oxo-3-pyrrolidinyl)methyl]formamide, 24744-92-1; N-benzyl-2,2-dibromoacetamide, 24744-94-3; **2a**, 24744-81-8; **2b**, 24744-82-9; **3**, 24744-83-0; **4**, 24744-84-1; **4a**, 24744-85-2; **5**, 24744-86-3; **6**, 24799-54-0; **7**, 24744-87-4; **8**, 24744-88-5; **9**, 24744-89-6; **13**, 24744-93-2.

(32) F. F. Blicke and C.-J. Lu, *J. Amer. Chem. Soc.*, **74**, 3933 (1952).
(33) C. Franconi, *Z. Elektrochem.*, **65**, 645 (1961).
(34) The authentic sample was prepared by treatment of dibromoacetyl chloride with benzylamine.

Pyrido[2′,1′:2,3]imidazo[5,1-*a*]isoquinolinium Cation[1]

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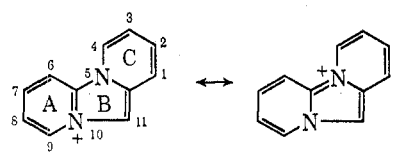
The first synthesis of the title cation has been effected *via* aromatic cyclodehydration of appropriately substituted 1-methylene-2-phenylimidazo[1,2-*a*]pyridinium bromides (**9** and **11**). The possibility that cyclization occurred in the pyrido ring (position 8) was excluded by showing that similar products (**3**) were obtained when position 8 was blocked with a methyl group.

Although the dipyrido[1,2-*a*:1′,2′-*c*]imidazolium cation (**1**)[2,3] and some of its benzologs[2,4,5] have been



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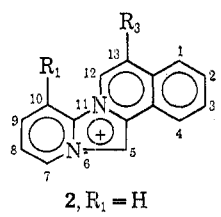
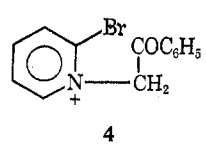
known for several years, the benzolog with the ring attached at positions 1 and 2 does not appear to have been reported. The synthesis of this benzolog, the pyrido[2′,1′:2,3]imidazo[5,1-*a*]isoquinolizinium cation (**2**) has now been accomplished.



2, R_1 = H
3, R_1 = CH_3



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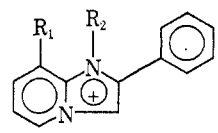
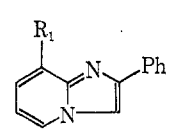
It has been shown[6] that, when certain amines are allowed to react with 2-bromo-1-phenacylpyridinium bromide (**4**), the product is a derivative of the 2-phenylimidazo[1,2-*a*]pyridinium ion (**5**). When the acetal of aminoacetaldehyde was allowed to react with the same quaternary salt (**4**), a product was obtained which was presumed to be impure 1-(2′,2′-diethoxyethyl)-2-phenylimidazo[1,2-*a*]pyridinium bromide (**6**). It would be expected that an acetal such as **6** would be hydrolyzed in hot mineral acid to the corresponding aldehyde (**9**, R_3 = H). In analogy to the behavior of 2-biphenylacetaldehyde[7] the resulting aldehyde would be expected



5, R_1 = H
6, R_1 = H; R_2 = $CH_2CH(OEt)_2$
9, R_1 = H; R_2 = CH_2COR_3
10, R_1 = H; R_2 = $CH{=}C(O^-){-}Ph$
11, R_1 = Me; R_2 = CH_2COR_3



7, R_1 = H
8, R_1 = CH_3

(1) This research was supported by Public Health Service Grant No. H-2170 of the National Heart Institute.
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(6) C. K. Bradsher, R. D. Brandau, J. E. Boliek, and T. L. Hough, *J. Org. Chem.*, **34**, 2129 (1969).
(7) C. K. Bradsher and W. J. Jackson, *J. Amer. Chem. Soc.*, **76**, 734 (1954).