The Reaction of Quaternary Pyridine Derivatives with Imidazoles*

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Diphosphopyridine nucleotide reacts chemically with a number of reagents, including alkali (1), cyanide (2, 3), bisulfite ions (2, 3), dihydroxyacetone (4), dithionite ions (5), hydroxylamine (6), mercaptans (7), and aromatic amines (8). All of these reagents are nucleophilic agents which react on a positive center. It is generally assumed that these reactions involve the addition of the nucleophilic agent to the position of the nicotinamide moiety where the hydrogen addition occurs during enzymatic or chemical reduction, i.e. the para position (9). This assumption has proved valid for the cyanide (10) and dithionite (5) addition reactions.

In one instance such an addition reaction seems to exist naturally. The binding of DPN to triosephosphate dehydrogenase from yeast or rabbit skeletal muscle results in an increased absorption in the region around 360 mp (11). This results in a spectrum of the enzyme-DPN complex which is similar to that of the addition complexes enumerated above. The analogue of DPN, acetylpyridine-DPN, shows this effect in a much more outstanding manner (12). It has been assumed (11, 7) that this spectral band represents a mercaptan addition to the DPN. However, two other groupings on the protein could conceivably interact with DPN and thus be responsible for such a spectrum. These are the imidazole group of histidine and the phenolic group of tyrosine.

The present paper describes the interaction which can exist between DPN and imidazoles.

EXPERIMENTAL

Pyridine Derivatives—DPN, acetylpyridine-DPN (13, 14), and pyridinealdehyde-DPN (13, 15) were products of the Pabst Laboratories. The latter two nucleotides were generously supplied by Dr. Nathan O. Kaplan.

The N-methyl pyridinium derivatives were prepared from the corresponding free bases by reaction with methyl iodide. The following were synthesized: N'-methyl-nicotinamide iodide, m.p. 201–202° (reported: 202.7–203.4° (16)); N'-methyl-3-acetylpyridinium iodide m.p. 155–156° (reported: 154.5–155.2° (17) and 163–164° (18)); N'-methyl-formamide-pyridinium iodide, m.p. 165–167° (reported: 164.5–166° (17), and 173° (18)); N'-methyl-3-carboxamide-pyridinium iodide, m.p. 149–151° (reported: 154–155° (18)); and N'-methyl-2-carboxamide-pyridinium iodide, m.p. 224–226° decomposition point (reported: 224–225° (18)).

Imidazole Derivatives—Imidazole, benzimidazole, 2-methyl benzimidazole, histamine, histidine, and l-methyl histidine were commercial preparations. All were used without further purification, with the exception of the oximes, which were prepared from the corresponding aldehydes (18).

N-benzyl-3-formyl-pyridinium bromide was an oil which could not be induced to crystallize. Previously the chlorides of N'-benzyl nicotinamide (19) and N-benzyl-3-acetylpyridine (20) have been reported.

The free pyridine bases were commercial preparations, with the exception of the oximes, which were prepared from the corresponding aldehydes (18).

Imidazole Derivatives—Imidazole, benzimidazole, 2-methyl benzimidazole, histamine, histidine, and l-methyl histidine were commercial preparations. All were used without further purification, with the exception of the 2-methyl benzimidazole which was recrystallized several times from water.

2-Imidazolone was prepared with 2-imidazolone-4-carboxylic acid by the method of Hilbert (21, 22). The product had a

* This investigation was supported in part by an institutional grant from the American Cancer Society.
† Investigator in the Howard Hughes Medical Institute.
1 All melting points were taken on a Fischer-Jones melting-point apparatus and are uncorrected.

The N-benzyl pyridinium derivatives were prepared, in essentially quantitative yields, by refluxing the pyridine base in either dry benzene or absolute ethanol with benzyl bromide. The compounds were recrystallized from ethanol or methanol. The following were prepared:


\[ \text{C}_{13}\text{H}_{13}\text{N}_{2}\text{OBr} (294.2) \]

Calculated: N 9.55

Found: N 9.62

2. N'-benzyl-3-carboxime-pyridinium bromide: very fine white needles, m.p. 184–187°.

\[ \text{C}_{13}\text{H}_{13}\text{N}_{2}\text{OBr} (294.2) \]

Calculated: N 9.55

Found: N 9.47


\[ \text{C}_{13}\text{H}_{13}\text{N}_{2}\text{OBr} (294.2) \]

Calculated: N 9.55

Found: N 9.43


\[ \text{C}_{13}\text{H}_{14}\text{NOBr} (291.2) \]

Calculated: N 4.79

Found: N 4.76

N-benzyl-3-formyl-pyridinium bromide was an oil which could not be induced to crystallize. Previously the chlorides of N'-benzyl nicotinamide (19) and N-benzyl-3-acetylpyridine (20) have been reported.
Imidazole and DPN

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1.0
0.8
0.6
0.4
0.2
0.0
0.1 1.0 1.5 2.0
IMIDAZOLE (MOLAR)

Fig. 1. The effect of imidazole and pyridine nucleotide concentration on the addition complex. Left, 0.1 M phosphate buffer, pH 10.0; imidazole concentration as indicated, and acetylpyridine-DPN, 500 µg. The final volume is 3.0 ml. Right, 0.1 M phosphate buffer, pH 10.0. The imidazole concentration is 0.7 M; pyridinealdehyde-DPN as indicated in a final volume of 3.0 ml.

8.0 9.0 10.0
11.0 12.0
PH

Fig. 2. The effect of pH on the reaction between imidazole and pyridine nucleotides with 0.1 M phosphate buffer, pH as indicated, 0.6 M imidazole, and 500 µg. of pyridinealdehyde-DPN. The observed extinctions are corrected for the effect of alkali on pyridinealdehyde-DPN. The final volume is 3.0 ml.

melting point of 249.5-250° (reported: 251-252° (23)). 2-Methyl imidazole was prepared from tartaric acid dinitrate (23), acetaldehyde and ammonia (24), m.p. 132-134° (reported: 134-136° (24)). The picrate was prepared from the free base: m.p. 206° (reported: 213° (25)). Alternately 2-methyl imidazole was prepared in low yield (10 per cent) as described for 2,4,5-trimethyl imidazole (26) by substitution of glyoxal for diacetyl. 4(5)-Tetrahydroxybutyl imidazole and carnosine were generous gifts of Dr. William J. Darby. Anserine and part of the 1-methyl histidine used were gifts from Dr. H. V. Aposhian.

Enzymes—Crystalline yeast alcohol dehydrogenase and crystalline rabbit skeletal muscle lactic dehydrogenase were purchased from the Worthington Biochemical Corporation. Crystalline α-glycerolphosphate dehydrogenase was prepared from rabbit skeletal muscle by the method of von Belsenherz et al. (27). Neurospora DPNase (28) was a generous gift of Dr. Anthony San Pietro. Pig brain DPNase was prepared by the method of Zatman et al. (29). As a source of rat liver DPNase, a 1:10 homogenate in 0.1 M phosphate buffer, pH 6.8, was used.

Determination—The concentration of pyridine nucleotides was determined by the reaction resulting from the addition of cyanide (3), or occasionally by alcohol dehydrogenase assay. The following molar extinction coefficients were used: for DPN, 6.3 x 10³ (30); for acetylpyridine-DPN, 7.8 x 10³ (13), and for pyridinealdehyde-DPN, 7.0 x 10³ (13, 15), all at their absorption maximum in the 300 to 400 mµ region.

Concentration of imidazole was determined by titrating an aliquot with standard acid, of inorganic phosphate by the method of Lowry and Lopez (31), and of total phosphate by the method of Fiske and SubbaRow (32). Ribose was estimated by the orcinol procedure (33) with the use of 5'-adenylic acid as a standard, and nicotinic acid was estimated by microbiological assay (34) with Lactobacillus arabinosus. The Pauly diazo reaction was performed by the method of McPherson (35). For the cyanogen bromide reaction the method of Dae and Ghosh was used (36).

RESULTS

Reaction of Imidazole with Pyridine Nucleotides

When DPN or DPN analogues were added to a solution containing imidazole, an increase in ultraviolet absorption occurred in the region of 300 to 400 mµ. The increase in absorption is dependent on the concentration of imidazole, the concentration of the pyridine nucleotide, and the hydrogen ion concentration. Figs. 1 and 2 illustrate these points for representative reaction mixtures.

As is the case with other addition reactions, acetylpyridine- DPN and pyridinealdehyde- DPN show a much more favorable addition reaction than does DPN.

Specificity of Reaction—This addition reaction is given by a variety of imidazole derivatives. Although for a number of those tested only indications of reactions were observed because of the limited amounts available, conclusive spectral evidence could be obtained with imidazole, 2-methyl imidazole, histamine,
histidine, and 4(5)-tetrahydroxybutyl imidazole. Benzimidazole and 2-methylbenzimidazole also showed evidence of the addition, but the complex seemed to be much weaker. Most reactions could be especially well observed in methanol as solvent, which obviates the requirement for a highly alkaline solution. 1-Methyl histidine and 2-imidazolone failed to interact under any of the conditions tried.

The addition reaction is also not limited to pyridine nucleotides. All quaternary pyridine derivatives tested show the reaction. Some of the absorption maxima observed when different compounds interact with imidazole derivatives are shown in Table I. A representative spectrum of an addition complex, that of the imidazole-acyethylpyridine-DPN complex, is shown in Fig. 3. It is interesting to note that again N-methylpyridinium derivatives have absorption maxima for their complexes approximately 10 μμ higher than those of the nucleotides.

As was shown for previous addition reactions, the quaternary nitrogen was essential for the interaction between pyridine and imidazole derivatives; pyridinediyaldehyde, acetylpyridine, or nico-tinamide fail to show any evidence for addition, even at high base concentration.

**Extinction Coefficients of Reaction Products**—When the molar extinction coefficients were measured at the maximal absorption for the imidazole-pyridine nucleotide complexes the following results were obtained: for the imidazole-DPN complex, 6.8 × 10⁴; for the imidazole-acetylpyridine-DPN complex, 1.18 × 10⁴; and for the imidazole-pyridinediyaldehyde-DPN complex, 1.39 × 10⁴. These extinction values are significantly higher than those observed for any other addition complex so far described.

**Equilibrium Constant of Reaction**—With the use of the above extinction coefficients the dissociation constant of the equilibrium, imidazole + pyridine nucleotide = complex + H⁺, could be determined. The complexes are weak, therefore some variation was observed, but the order of magnitude is correct. The following values were obtained: for DPN, 1.23 ± 0.6 × 10⁻¹⁷; for acetylpyridine-DPN, 2.8 ± 1.2 × 10⁻¹⁶; and for pyridinediyaldehyde-DPN, 1.2 ± 0.02 × 10⁻¹⁷. The average figures with their standard deviations are given. These figures indicate that again the order of ease of addition is: DPN, the least favorable; ADPR, intermediate; and ATPR, the most favorable; and acetylpyridine-DPN, intermediate.

The N-methyl derivatives are much less favorable in their addition than are the nucleotides, whereas the N-benzyl derivatives seem to be intermediate between these extremes.

**Effect of Ferricyanide on Complexes**—Since imidazole is relatively stable to oxidation, it was feasible to prepare the oxidized analogues of the imidazole addition complexes by treatment with ferricyanide. This is entirely analogous to the synthesis of the oxidized dihydroxyacetone addition complexes (37, 38).

The reaction could readily be followed by measurement of the ferri-ferricyanide formed after addition of aliquots taken from the reaction mixture to a solution containing ferro sulfate. Such an experiment is shown in Fig. 4. As can be seen, it was not essential to free the complex from excess imidazole. By this method it has been possible to isolate oxidized imidazole complexes in pure form.

**Preparation of 1-Methyl-3-acetyl-4-(1-imidazoly)-pyridinium Reineckate**—1.26 gm. (5 mmoles) of N-methyl-3-acetylpyridinium iodide, 1.36 gm. (20 mmoles) of imidazole, and 2.0 gm. (6 mmoles) of potassium ferricyanide were dissolved in 30 ml. of distilled water. The mixture was cooled in ice, stirred by a stream of nitrogen, and kept slightly alkaline by the cautious dropwise addition of 0.40 gm. (7 mmoles) of potassium hydroxide dissolved in 10 ml. of distilled water. Great care was taken to avoid a local excess of base. When the reaction was complete, as was determined by ferrocyanide formation (2.5 hours), 10 ml. of a saturated solution of Reinecke salt in methanol were added. The mixture was allowed to stand for 1 additional hour in the cold in order to complete crystallization. The crystals were filtered off, and washed first with small portions of ice-cold

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**Table I**

<table>
<thead>
<tr>
<th>Pyridine derivative</th>
<th>Nitrogen substituent</th>
<th>Other ring substituent</th>
<th>Imidazole</th>
<th>Histidine</th>
<th>Histonine</th>
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<tr>
<td>Methyl</td>
<td>3-Carboxamide</td>
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<td>3-Acetyl</td>
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<td></td>
<td>3-Formyl</td>
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<td>335</td>
<td>335</td>
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<tr>
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<td>3-Carboxime</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
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<tr>
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<td>2-Carboxime</td>
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<tr>
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<tr>
<td></td>
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<td>340</td>
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<td>350</td>
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<tr>
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<td>305</td>
<td>305</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3-Acetyl</td>
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<td>330</td>
<td>330</td>
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<td>3-Formyl</td>
<td>325</td>
<td>325</td>
<td>325</td>
<td>325</td>
</tr>
</tbody>
</table>

* The reaction is too unfavorable to observe the addition complex.
† The alkali shift in spectrum completely obscures the addition reaction.
‡ ADPR stands for the adenosine diphosphate ribose moiety of DPN, and ATPR stands for the adenosine diphosphate ribose phosphate moiety of TPN.
§ In phosphate buffer histamine seems to destroy pyridinealdehyde-DPN. On mixing of pyridinealdehyde-DPN and histamine in phosphate buffer, pH 10.5, an initial sharp peak appears which subsequently disappears rapidly.
water and then with n-propanol. The isolated salt was recrystallized by suspension in a small amount of hot water to which acetone was added until just dissolved. The compound was a microcrystalline orange powder. The yield was 1.2 gm. (45 per cent), m.p. 152-155° decomposition point (authentic N-methyl-3-acetyl-pyridinium reineckate melts at 144-146°, mixed m.p. with the product is 141-143°). The compound analyzed as a dihydrate as follows:

\[
C_{13}H_{21}O_7S_2Cr·2H_2O \quad (559.7)
\]

Calculated: C 32.2, H 4.5, N 22.6, Cr (as CrO₃) 17.8

Found: C 32.1, H 4.6, N 21.3, Cr (as CrO₃) 17.5

The reineckate could be suspended in water and treated with a suspension of Dowex 1-chloride to yield a yellow solution of 1-methyl-3-acetyl-4-(1-imidazolyl)-pyridinium chloride. Ultraviolet absorption spectra showed in 0.2 n HCl or neutral solutions a maximum at 265 m\(\mu\) and a shoulder at 275 m\(\mu\). In 0.1 n KOH a maximum at 270 m\(\mu\) and a second maximum at 332 m\(\mu\) were observed. The minimum was at 295 m\(\mu\).

Preparation of \(p\)-(1-Imidazolylj-DPN (Imidazole-DPN)—The reaction mixture, as described in Fig. 4, could be placed on a column of Dowex 1-formate form. For 600 mg. of DPN a column was used with dimensions of 3 \(\times\) 10 cm. The column was washed thoroughly with water until all the imidazole was eluted. Ferri- and ferrocyanide were held tenaciously to the resin. Gradient elution with formic acid gave a sharp peak (as was determined by absorption at 260 m\(\mu\) of the eluates) of imidazole-DPN at approximately 0.07 m formic acid. The appropriate fractions were combined and lyophilized to yield 200 mg. of an extremely fluffy powder. Paper chromatography indicated that the material was essentially homogeneous in two solvents tested: (a) ethanol and 0.1 n acetic acid (1:1); (b) isobutyric acid, concentrated NH₄OH, and water (66:1:33). The \(R_f\) value was identical to that of DPN.

Spectral Properties of Imidazole-DPN—The ultraviolet spectra of imidazole-DPN are shown in Fig. 5. It is of interest that the substance still interacts with cyanide; the maximum is, however, shifted from 325 m\(\mu\) for DPN to 335 m\(\mu\) for imidazole-DPN. A sample of imidazole-DPN was converted by nitrous acid treat-
color, 1-methyl histidine and anserine did not. It is of interest that 2-methyl imidazole does give a diazo reaction under these conditions.

Upon treatment with hot alkali, imidazole-DPN gives a strongly fluorescent product similar to DPN, with a maximal absorption at 370 mp. Autoclaving the nucleotide at pH 7.0 yields a substance with growth-promoting activity for L. arabinosus in a 60 to 95 per cent yield.

The titration curve of the nucleotide shows only one dissociation between pH 2.0 and 8.5. This dissociation has a pK of 3.7 and presumably reflects the adenine amino group.

**Enzymatic Properties of Imidazole-DPN**—Imidazole-DPN fails to replace DPN for crystalline yeast alcohol dehydrogenase, crystalline muscle lactic dehydrogenase, or crystalline muscle cytochrome c by glycerol phosphate dehydrogenase. Also, in concentrations up to 50 times that of DPN, no inhibitory action can be observed.

*Neurospora* DPNase also fails to attack the new nucleotide. However, this enzyme is 20 per cent inhibited by equimolar concentrations of DPN and imidazole-DPN. Pig brain DPNase and rat liver DPNase, on the other hand, both attacked the imidazole-DPN. The rates of breakdown were respectively 40 and 10 per cent of that of DPN. Nicotinamide at concentrations up to 0.2 m promoted little or no DPN resynthesis from imidazole-DPN by the exchange reaction which these enzymes can catalyze (43, 44). This is analogous to the behavior of acetylpyridine-DPN, which is a good substrate for pig brain DPNase, but one which cannot be converted back to DPN through a nicotinamide-acetylpyridine exchange (13).

**Products of Enzymatic Breakdown of Imidazole-DPN**—When the reaction mixture of DPN and pig brain DPNase was chromatographed on filter paper (Whatman No. 4) with the use of the solvent of ethanol and 0.1 n acetic acid (1:1), two new spots appeared as a result of the action of the enzyme. The incubation mixture of DPN and the enzyme was used for comparison. In this solvent system DPN and imidazole-DPN have identical RF values at 0.43. The first spot, which was a result of the breakdown of imidazole-DPN, had an RF of 0.53 and corresponded to adenosine diphosphate ribose. The spot was eluted from the paper and found to be devoid of cyanide-reactive material. It contained adenine, ribose, and phosphate in an approximate ratio of 1:2:2.

### Table II

**Chemical analysis of oxidized imidazole-DPN complex**

<table>
<thead>
<tr>
<th></th>
<th>Imidazole-DPN</th>
<th>Deaminoimidazole-DPN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotinamide</td>
<td>0.97</td>
<td>0.90</td>
</tr>
<tr>
<td>Cyanide</td>
<td>0.90</td>
<td>0.80</td>
</tr>
<tr>
<td>Microbiological</td>
<td>0.91</td>
<td>0.91</td>
</tr>
<tr>
<td>Adenine</td>
<td>1.50</td>
<td>1.70</td>
</tr>
<tr>
<td>Ribose</td>
<td>2.13</td>
<td>2.00</td>
</tr>
<tr>
<td>Phosphate</td>
<td>0.13</td>
<td>0</td>
</tr>
<tr>
<td>Inorganic</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Organic*</td>
<td>2.00</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>2.13</td>
<td>2.00</td>
</tr>
<tr>
<td>DPN</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ratio of phosphate to ribose to nicotinamide</td>
<td>1:0.75:0.48</td>
<td>1:0.85:0.40</td>
</tr>
</tbody>
</table>

* Absolute analysis, corrected for inorganic phosphate, yielded the following results for imidazole-DPN:

\[
C_{4}H_{3}O_{6}N_{7}O_{7} \cdot 2H_{2}O (731.5)
\]

Calculated: P 8.3, \(H_{2}O\) 4.80

Found: \(P 8.3, H_{2}O 4.85\)
The reaction was followed by withdrawing at intervals 0.1 ml. of the mixture and adding this to 3.0 ml. of 1 M potassium cyanide. The decrease in extinction at 335 m\(\mu\) was an indication of the hydrolysis. After 1 hour, 60 per cent was hydrolyzed. The tube was placed in a boiling water bath for 3 minutes, the precipitated proteins were removed by centrifugation, and the supernatant was passed over a Dowex 1-chloride column (3 X 1 cm.) after adjusting the pH to 7.8 with disodium hydrogen phosphate. The percolate and 10 ml. of distilled water, used to wash the column, were combined and evaporated to dryness. The residue was taken up in a suitable volume. Left, the ultraviolet spectrum of the base. 0.2 N HCl, O----O, 0.2 N KOH, O----O, 1 M KCN, A---A. For comparison the spectrum of nicotinamide at half concentration is shown: 0.2 N HCl, A---A, 1 M KCN or 0.2 N KOH, O----O.

Right, spectrum of the cyanogen bromide reaction mixture. The curve with solid circles, for comparison, represents the absorption spectrum of a mixture containing nicotinamide.

The second new spot arising from imidazole-DPN had an \(R_f\) of 0.80. Nicotinamide in the control incubation mixture had and \(R_f\) of 0.73. This compound, presumably 3-carboxamide-4-(1-imidazolyl)-pyridine, had the spectral characteristics shown in Fig. 6. Larger quantities of the base could be obtained by passing the incubation mixture through a column of Dowex 1-chloride, as described in the figure. The new base was shown to be a tertiary pyridine base by the reaction with cyanogen bromide.

It is of special interest that the cyanogen bromide produced a chromophore which is not grossly different from the one resulting from nicotinamide, although the ultraviolet spectrum is distinctly different. This suggests addition to the pyridine ring rather than alteration of the ring. It is of interest in this respect that the absorption maximum of 1-methyl histidine in allaline at 222 m\(\mu\) is shifted in cyanide to 230 m\(\mu\). This shows an interaction between cyanide ion and substituted imidazole rings.

**DISCUSSION**

The strong interaction of the quaternary pyridinealdoximes with imidazoles is of special interest. Derivatives of this nature are used as reactivators of organophosphate-inhibited proteinases and esterases (45-47). Recent speculations as to the mechanism of hydrolysis by chymotrypsin (48) implicate the proximity of a serine hydroxyl and an imidazole nucleus as the active center of the enzyme. Favorable binding of the quaternary pyridinealdoximes by the imidazole in the active center may therefore contribute to their reactivating power.

The structure of the reaction product of ferricyanide oxidation of the DPN-imidazole complex as p-(1-imidazolyl)-DPN is based upon the following evidence. The new nucleotide has the adenosine diphosphate ribose moiety still intact, which is shown by the unchanged pK of the adenine-amino group, the conversion of the adenine spectrum into a hypoxanthine spectrum by nitrous acid, and the actual isolation of adenosine diphosphate ribose from the action of pig brain DPNase on the molecule. That the nicotinamide ring has not been oxidized to a pyridine is shown by the recovery of nicotinic acid with growth-promoting activity for \(L.\) arabinosus, the absence of pyridone spectral characteristics, and the positive cyanogen bromide reaction of the pyridine base. The substitution of the ring in the para position is based on analogy to other addition reactions and to the high rate of hydrolysis of the analogue by pig brain DPNase; 2- or 6-substituted derivatives would be expected to give a much slower rate of hydrolysis. Also, substitution at the 2 or 6 position would be expected to give entirely different chromophores after the opening of the ring by cyanogen bromide.

The substitution on the 1 position of the imidazole ring is in-
...dialed by the following points. First, the imidazole-DPN fails to show a reaction with diazotized sulfanilic acid; this is similar to the case of 1-methyl imidazole derivatives, whereas 2-methyl derivatives do react. Furthermore, an addition reaction between DPN and imidazole derivatives can be seen with a variety of 2-, 4-, or 5-substituted imidazoles: histidine, histamine, 2-methyl imidazole, benzimidazole, and 2-methyl benzimidazole. On the other hand, 1-methyl histidine fails to react. Thus a reaction at the 1 (3) nitrogen atom seems indicated. This nitrogen has to be a secondary amine, as is indicated by the failure of addition complexes.

1-carboxime-pyridinium iodide is discussed with reference to the interaction between diphosphopyridine nucleotide and the probable pyridine nucleotide derivative. The properties of this new analogue of diphosphopyridine nucleotide and the probable structure are described and discussed.

4. The interaction observed between imidazole and N-methyl-2-carboxymy-pyridinium iodide is discussed with reference to the ability of this pyridine base to reactivate enzymes inhibited by organophosphorus compounds.

REFERENCES

The Reaction of Quaternary Pyridine Derivatives with Imidazoles
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