Cleavage of 2-Propoxypyridine with Concentrated Hydrobromic Acid.—A mixture of 3.5 g. of 2-propoxypyridine and 100 ml. of 42% hydrobromic acid was refluxed for six hours. It was then concentrated by distillation to a volume of 10 ml. This was made neutral to litmus paper with concentrated sodium hydroxide solution and extracted with three 20-ml. portions of ether. The ether solution which should contain the starting material was evaporated. Only a negligible residue remained. The aqueous solution was evaporated to a moist residue and extracted once with 15 ml. of boiling acetone. To this was added a saturated solution of picric acid in 15 ml. of acetone. On cooling in an ice-bath for one hour, a solid mass of yellow needles formed, yield 5.1 g. (61%). The melting point was 171–174° (cor.), and the product proved to be 2-pyridone picrate.

Attempted Cleavage of N-*n*-Propyl-2-pyridone with Concentrated Hydrobromic Acid.—A mixture of 3.5 g. of N-*n*-propyl-2-pyridone and 100 ml. of 42% hydrobromic acid was refluxed for six hours. It was then concentrated by distillation to a volume of 10 ml. This was neutralized to litmus paper with concentrated sodium hydroxide solution and the two layers separated. The aqueous layer was extracted with three 20-ml. portions of isoamyl alcohol. The extracts were combined with the top layer, dried over anhydrous magnesium sulfate and distilled. The product boiling from 245–255° was collected. The recovery was 2.9 g. (82%). The aqueous layer was then treated in a manner similar to that mentioned under the cleavage of 2-propoxypyridine. No 2-pyridone picrate was obtained.

Summary

1. N-*n*-Propyl-2-pyridone and the *n*-propyl ether of 2-hydroxypyridine have been synthesized and subjected to the action of boiling hydrobromic acid. The former is unchanged but the latter is hydrolyzed to 2-pyridone.

2. β-(N-2-Pyridone)-propionic acid, a compound analogous to that proposed for leucenol, was prepared in two ways: (1) from sodium 2-pyridone and β-chloropropionic acid, (2) from sodium pyridone and acrylonitrile followed by hydrolysis. This propionic acid cleaves by pyrolysis to 2-pyridone and acrylic acid; it is unaffected by boiling with aqueous hydrobromic acid; it is cleaved by strong alkali to 2-pyridone.

3. The data presented above with those previously reported support the assumption that leucenol has its side chain attached to the nitrogen of a pyridone rather than to the oxygen of an hydroxypyridine.

URBANA, ILLINOIS RECEIVED FEBRUARY 8, 1947

[CONTRIBUTION FROM THE DEPARTMENT OF RESEARCH IN PURE CHEMISTRY, MELLON INSTITUTE]

On the Structure of Leucaenine (Leucaenol) from *Leucaena glauca* Bentham. II.

BY A. F. BICKEL[1]

On pyrolysis of leucaenine, an amino acid occurring in the tropical plant, *Leucaena glauca* Bentham, Adams, *et al.*,[2] obtained a dihydroxypyridine. Because the properties of this compound differed from those of all five known dihydroxypyridines reported in the literature, Adams, *et al.*,[2] assumed their compound to be the still-unknown 2,5-dihydroxypyridine. Wibaut and Kleipool,[3] and Bickel[4] proved that a compound obtained by Bickel and Wibaut[5] on degradative methylation (of leucaenine) is a derivative of 3,4-dihydroxypyridine. Hence it seemed very probable that the dihydroxypyridine isolated by Adams, *et al.*,[2] actually has the 3,4-structure. Experiments clearly demonstrating the identity of synthetic 3,4-dihydroxypyridine with the compound obtained on pyrolysis have now been completed. Both substances have the same melting point; the aqueous solutions of both are neutral to litmus, and give the same color reaction with ferric chloride; and both compounds react with acetic anhydride to form diacetates, which are also identical in all respects. These properties correspond closely with those reported by Adams, *et al.*[2]

3,4-Dihydroxypyridine was synthesized by hydrolysis of 3-methoxy-4-hydroxypyridine, using a method somewhat different from that described by Peratoner.[6]

The results obtained in the present investigation offer further support for assigning the 3,4-structure to leucaenine.[4]

Experimental

All melting points given are corrected.

3-Methoxy-4-hydroxypyridine was prepared by heating 3.02 g. of 3-methoxypyrone-4[4] with 125 cc. of 6% ammonia on the steam-bath for two hours.[7] The excess ammonia was then removed by evaporation on the steam-bath, the residue dissolved in water, and the solution boiled with Nuchar W. On cooling the filtrate, colorless crystals separated out. The product was filtered off and washed with a small quantity of ice-water. The air-dried trihydrate (yield, 2.92 g.; 68%) melted at 119° on rapid heating; Peratoner[7] gave m. p. 114°. Recrystallization from ethanol, and drying over phosphorus pentoxide, yielded 1.84 g. of 3-methoxy-4-hydroxypyridine, m. p., 180.5–181.5°. Peratoner[7] gave m. p. 173°.

Anal.[8] Calcd. for $C_6H_7O_2N$: C, 57.58; H, 5.64. Found: C, 57.62; H, 5.79.

3,4-Dihydroxypyridine. A. From 3-Methoxy-4-hydroxypyridine.—3-Methoxy-4-hydroxypyridine trihydrate (4.55 g.) was heated with 50 cc. of 38% hydrochloric acid in a sealed tube at 145° for five hours. The excess hydrochloric acid was removed by evaporation *in vacuo* and the residue was thoroughly dried in the vacuum desiccator over

(1) Visiting Fellow, Netherland-America Foundation.

(2) Adams, Cristol, Anderson and Albert, THIS JOURNAL, **67**, 89 (1945).

(3) Wibaut and Kleipool, *Rec. trav. chim.*, **66**, 24 (1947); Wibaut, *Helv. Chim. Acta*, **29**, 1669 (1946).

(4) Bickel, THIS JOURNAL, **69**, 1801 (1947).

(5) Bickel and Wibaut, *Rec. trav. chim.*, **65**, 65 (1946).

(6) Peratoner, *Gazz. chim. ital.*, **36**, I, 56 (1906).

(7) Peratoner, *ibid.*, **36**, I, 52 (1906).

(8) The microanalyses were carried out by Mr. G. L. Stragand of the University of Pittsburgh.

potassium hydroxide. The slightly discolored crystals obtained were dissolved in 15 cc. of water; the solution was heated to 80° and neutralized with lithium carbonate, 101% of the theoretical quantity being necessary to reach pH 7. On cooling, the colorless needles which separated were filtered off, washed twice with 3-cc. portions of ice-water, and dried at 60°. Yield was 2.72 g. (96%); m. p., 239.5–240°, decomposition above 230°.

Anal. Calcd. for $C_5H_5O_2N$: C, 54.03; H, 4.54; N, 12.61. Found: C, 54.34; H, 4.58; N, 12.68.

The aqueous solution of a test sample was neutral to litmus and gave a violet color with ferric chloride.

The **diacetate** was prepared by the method of Adams, *et al.*[2] The dihydroxypyridine (130 mg.) was heated with 1.0 cc. of acetic anhydride for five minutes. Excess acetic anhydride and acetic acid were removed in a vacuum desiccator over potassium hydroxide. The almost-colorless residue was recrystallized (Nuchar W) from dry ethyl acetate, yielding shiny leaflets, m. p., 138.5–140°.

Anal. Calcd. for $C_9H_9O_4N$: C, 55.38; H, 4.65; N, 7.18. Found: C, 55.65; H, 4.88; N, 7.16.

The aqueous solution of a test sample was neutral and gave no color with ferric chloride. On standing, however, the reaction became acid and a violet color was developed with ferric chloride.

A **monoacetate** was isolated when the crude acetylation product was allowed to stand in a vacuum desiccator over potassium hydroxide for fourteen days. Upon extraction with boiling ethyl acetate, a small quantity of the monoacetate remained undissolved; colorless needles, m. p., 145.5–146.5°.

Anal. Calcd. for $C_7H_7O_3N$: N, 9.15. Found: N, 9.30.

The aqueous solution of a test sample gave no color with ferric chloride. On standing, however, a violet color developed. This behavior indicates that the 3-monoacetate has been isolated. Apparently, this compound is not identical with the monoacetate described by Peratoner,[6] m. p. 207–208°.

B. From Leucaenine.—Two grams of leucaenine were pyrolyzed in a vacuum sublimation apparatus at 200–240° (1 mm.).[3] The sublimate (900 mg.) was recrystallized twice from water (Nuchar W), giving colorless crystals which were dried at 60°. Yield was 390 mg.; m. p., 239.5–240°, decomposition above 230°.

Anal. Calcd. for $C_5H_5O_2N$: C, 54.03; H, 4.54; N, 12.61. Found: C, 53.80; H, 4.35; N, 12.90.

Mixed melting point with 3,4-dihydroxypyridine from A was 239.5–240°, decomposition above 230°.

The **diacetate** was prepared as described above: colorless leaflets, m. p., 139–140°.

Anal. Calcd. for $C_9H_9O_4N$: C, 55.38; H, 4.65; N, 7.18. Found: C, 55.51; H, 4.36; N, 7.35.

Mixed melting point with the diacetate from A, was 138.5–140°.

Summary

The dihydroxypyridine obtained when leucaenine is pyrolyzed (in the manner described by Adams, *et al.*) has been proved to have the 3,4-structure.

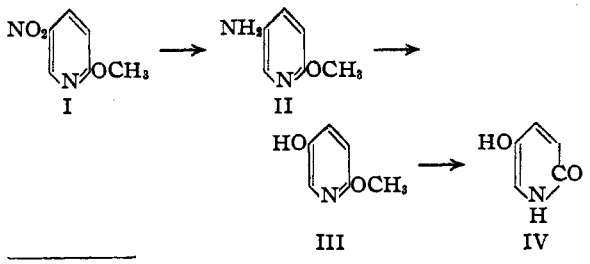
PITTSBURGH 13, PA. RECEIVED FEBRUARY 27, 1947

[CONTRIBUTION FROM NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Structure of Leucenol. III. Synthesis of 2,5-Dihydroxypyridine (5-Hydroxy-2-pyridone)[1]

BY ROGER ADAMS AND T. R. GOVINDACHARI

By the pyrolysis of leucenol, a dihydroxypyridine (hydroxypyridone) was isolated which was assumed to be the unknown 5-hydroxy-2-pyridone because its properties did not conform to those described in the literature for any of the five known isomers. In this Laboratory and in that of Wibaut[2] previous attempts to prepare this compound have failed. A successful synthesis of 5-hydroxy-2-pyridone has now been realized. It is a stable compound resembling the other hydroxypyridones. 2-Methoxy-5-nitropyridine (I) was reduced to the corresponding amino compound (II). This was diazotized and the amino group replaced by hydroxyl to yield 2-methoxy-5-hydroxypyridine (III) which hydrolyzed readily in the presence of hydrobromic acid to give 2,5-dihydroxypyridine (5-hydroxy-2-pyridone) (IV). The yields in all steps except the replacement of the amino group by hydroxyl were very satisfactory. In general diazotization of a 3-aminopyridine gives low yields[3] but in this case only 3–4% yield resulted. No attempts to improve this preparation were made since the amount of 2-methoxy-5-hydroxypyridine obtained was adequate for hydrolysis and characterization of the 5-hydroxy-2-pyridone. The 2-methoxy-5-aminopyridine is reported in the literature both as a crystalline solid,[4] m. p. 135–136°, and as an oil extremely susceptible to oxidation.[5] In this investigation it proved to be a colorless oil easily obtainable in quantitative yields.



I II III IV

The pyridone (IV) begins turning dark at 215° and decomposes without melting at 240–250° (cor.) and a mixture with the leucenol pyrolysate (m. p. 242–244° with decomposition), melts at 210° with decomposition. The synthetic product gives a pinkish red color with ferric chloride, un-

(1) For previous paper see Adams and Jones, THIS JOURNAL, **69**, 1803 (1947); Paper V, *ibid.*, **69**, 1810 (1947).

(2) Bickel and Wibaut, *Rec. trav. chim.*, **65**, 65 (1946).

(3) Schickh, Binz and Schulz, *Ber.*, **69**, 2600 (1936); Parker and Shive, THIS JOURNAL, **69**, 63 (1947).

(4) Rath, *Ann.*, **484**, 52 (1930).

(5) Magidson and Menschikoff, *Ber.*, **58**, 113 (1925).