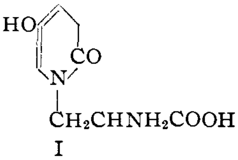
[CONTRIBUTION FROM NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

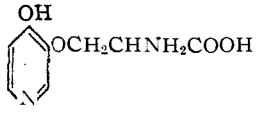
The Structure of Leucenol. IV

BY ROGER ADAMS, V. V. JONES AND J. L. JOHNSON

The structures for leucenol which have been previously proposed are shown in formulas I,[1] II,[2] III[2] and IV.[3]



I



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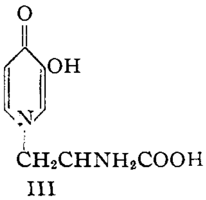

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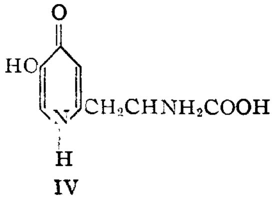

IV

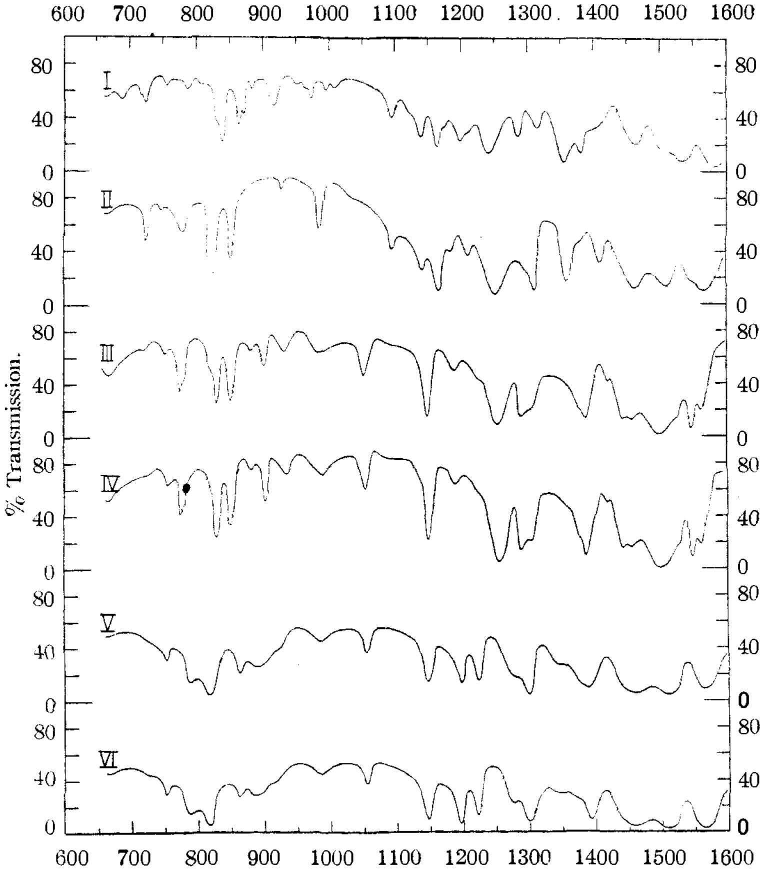

Fig 1.—Infrared absorption spectra of: I, leucenol: II, N-methyl-3-hydroxy-4-pyridone; III, 3-hydroxy-4-pyridone; IV, leucenol pyrolysate; V, 3-hydroxy-4-pyridone monohydrate; VI, leucenol pyrolysate monohydrate. All spectra were run in Nujol which shows C–H bands at 2920 and 2850 cm.$^{-1}$, and at 1460 and 1375 cm.$^{-1}$.

The evidence presented in a previous paper[1b] eliminates II from consideration and the recent synthesis[4] of 5-hydroxy-2-pyridone makes formula I impossible. Formula IV is very unlikely in view of the elimination of the side chain in leucenol either by pyrolysis or by the action of strong alkali. Formula III, suggested by Wibaut, must therefore be accepted as most probably correct. Wibaut[2] obtained a monomethylated degradation product from leucenol which he demonstrated was N-methyl-3-hydroxy-4-pyridone. He postulated that his dimethylated degradation product was

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[1] (a) Adams, Cristol, Anderson and Albert, THIS JOURNAL, **67**, 89 (1945); (b) Adams and Jones, *ibid.*, **69**, 1803 (1947).

[2] Bickel and Wibaut, *Rec. trav. chim.*, **65**, 65 (1946); Wibaut, *Helv. Chim. Acta*, **29**, 1669 (1946). See also Wibaut and Kleipool, *Rec. trav. chim.*, **66**, 24 (1917).

[3] Kostemans, *Rec. trav. chim.*, **65**, 319 (1946); **66**, 93 (1947).

[4] Adams and Govindachari, THIS JOURNAL, **69**, 1806 (1947).

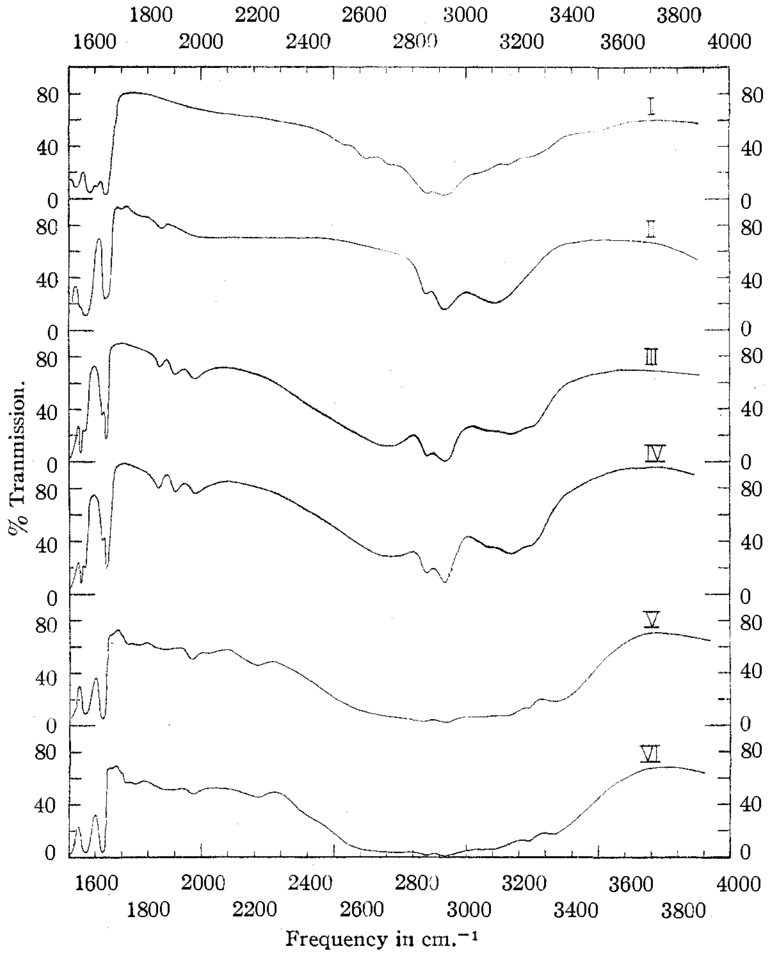

Fig. 2.—Infrared absorption spectra of: I, leucenol; II, N-methyl-3-hydroxy-4-pyridine; III, 3-hydroxy-4-pyridone; IV, leucenol pyrolysate; V, 3-hydroxy-4-pyridone monohydrate; VI, leucenol pyrolysate monohydrate. All spectra were run in Nujol which shows C–H bands at 2920 and 2850 cm.$^{-1}$ and at 1460 and 1375 cm.$^{-1}$.

N-methyl-3-methoxy-4-pyridone and a recent synthesis by Bickel[5] has confirmed this fact.

The pyrolysis product of leucenol has been prepared again. Upon repeated crystallization it was obtained perfectly colorless but had the same melting point, 242–244°, previously reported. The synthesis of the diacetate and its analysis confirmed former results. Not observed before was the formation of an unstable hydrate upon crystallization from water. Upon methylation with excess diazomethane, a product was obtained, m. p. 91–92°, which proved identical with N-methyl-3-methoxy-4-pyridone monohydrate by a melting point of the mixture with an authentic sample of the latter. It is thus obvious that the leucenol pyrolysate is 3-hydroxy-4-pyridone.

The preparation of 3-hydroxy-4-pyridone by the procedure of Peratoner and Tamburello[6] was duplicated with minor modifications. The product obtained, however, had identical properties with leucenol pyrolysate and not those assigned to it by the Italian investigators.

The ultraviolet absorption spectra of leucenol and several pyridones have been determined and are shown in Figs. 1 and 2.

It may be seen that the unsubstituted 4-pyridone or N-methyl-4-pyridone absorbs at about 2400 Å. while the unsubstituted 2-pyridone or N-methyl-2-pyridone absorbs at 2800 Å. On the other hand, the presence of an hydroxyl in a 4-pyridone molecule shifts the absorption of the 4-pyridones to a position close to that of the 2-pyridones. Thus, leucenol, N-methyl-3-hydroxy-4-pyridone and 3-hydroxy-4-pyridone (leucenol pyrolysate) show similar absorption to each other and to unsubstituted 2-pyridones.

The infrared absorption spectra of leucenol, leucenol pyrolysate, hydrated and anhydrous, 3-hydroxy-4-pyridone, hydrated and anhydrous and N-methyl-3-hydroxy-4-pyridone are given in Fig. 3.

The authors are indebted to J. C. Brantley for

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[5] Bickel, THIS JOURNAL, **69**, 1801 (1947).

[6] Peratoner and Tamburello, *Gazz. chim. ital.*, **36**, I, 55 (1906).

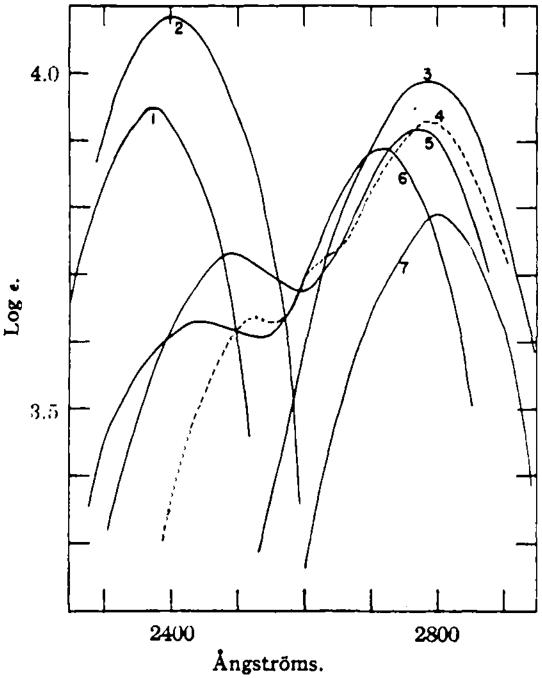

Fig. 3.—Curves 1 and 2 are from Specker and Gavrosch, *Ber.*, **75B**, 1338 (1942). The leucenol (25 mg.) was dissolved in 50 ml. of 0.1 *N* HCl in water and diluted 25 times with 0.1 *N* HCl in methanol. The other compounds were dissolved directly in 0.1 *N* HCl in methanol: 1, 4-pyridone; 2, N-methyl-4-pyridone; 3, 2-pyridone; 4, leucenol; 5, N-methyl-3-hydroxy-4-pyridone; 6, leucenol pyrolysate; 7, N-methyl-2-pyridone.

the ultraviolet absorption determinations and to Mrs. Agatha R. Johnson for the infrared absorption determinations.

Experimental

Leucenol.—The procedure of Kostermans[8] for extracting the alkaloid was found superior to that used in this Laboratory[1] or by Wibaut.[3]

Leucenol Pyrolysate.—This product was made as previously described and formed colorless needles from ethanol, m. p. 242–244°. From water it formed white needle clusters which contained one molecule of water of crystallization. The hydrated form lost its water without melting.

Anal. Calcd. for $C_5H_5O_2N \cdot H_2O$: H_2O, 11.96. Found: H_2O, 11.92.

In aqueous solution, minimum quantities of ferric chloride solution produce a red color which changes to purple on addition of more reagent. In aqueous solution it is neutral to litmus. Acetylation gives a diacetate as previously described.[1]

Methylation of Leucenol Pyrolysate.—One-tenth gram of leucenol pyrolysate was pulverized and allowed to stand in an excess of diazomethane in 50 ml. of cold ether at room temperature for two hours. The excess diazomethane and solvent was evaporated on a hot water-bath. The brown-colored sirup remaining was dried in a vacuum desiccator and extracted with dioxane; colorless crystals, m. p., 91–92°. A melting point of the mixture with N-methyl-3-methoxy-4-pyridone monohydrate prepared by the action of methylamine on 3-methoxy-4-pyrone showed *no* depression.

3-Hydroxy-4-pyridone.—A mixture of 0.7 g. of 3-methoxy-4-pyridone[6] and 40 ml. of a concentrated solution of hydriodic acid was refluxed for one and one-half hours while a stream of carbon dioxide was passed through. Most of the hydriodic acid was distilled off in a stream of carbon dioxide and the residue steam-distilled to remove the iodine. The resulting sirup was made just neutral with aqueous sodium hydroxide and evaporated to dryness. The residue was pulverized and sublimed at 200° at 1 mm. The yield of product was 0.30 g. (50%). It was purified by recrystallization from 95% ethanol, m. p. 242–244° (cor.). A melting point of the mixture with leucenol pyrolysate showed no depression. From water, it takes up water of crystallization.

Anal. Calcd. for $C_5H_5O_2N$: C, 54.07; H, 4.50; N, 12.61. Found: C, 54.03; H, 4.60; N, 12.65.

It has the same properties as those described for the leucenol pyrolysate.

N-Methyl-3-methoxy-4-pyridone.—A mixture of 50 cc. of 10% aqueous solution of methylamine and 0.85 g. of 3-methoxy-4-pyrone was refluxed for two hours, then evaporated to dryness on a steam-bath. The residue was extracted with boiling dioxane and the product recrystallized from the same solvent; white crystals, m. p. 91–92° (cor.).

Anal. Calcd. for $C_7H_9O_2N \cdot H_2O$: C, 53.52; H, 7.07; N, 8.92; H_2O 11.45. Found: C, 53.76; H, 6.82; N, 8.78; H_2O, 11.15.

Summary

1. Leucenol pyrolysate was obtained as colorless crystals which from water takes up one molecule of water of crystallization.

2. This product on methylation with diazomethane gives N-methyl-3-methoxy-4-pyridone and therefore must be 3-hydroxy-4-pyridone.

3. 3-Hydroxy-4-pyridone was prepared by the method of Peratoner and shown to have properties different from those described by him but identical with those of the leucenol pyrolysate.

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