on a slurry of ice and dilute sulfuric acid. The oil which separated in large amount crystallized in a few seconds, but upon warming to room temperature during filtration and washing, it deflagrated vigorously. In subsequent preparations, it was therefore taken up in cold benzene and dried and handled in that solvent. Treatment of such a benzene solution with hydrogen chloride in dioxane gave no crystallizable product. Treatment with alcoholic sodium hydroxide yielded less than 5% of octahydrophenazine. *p*-Toluenesulfonylphenylacetoxime likewise gave no crystalline products when treated with hydrogen chloride in dioxane.

Summary

1. The potassium oxime-O-sulfonates of eight ketones have been prepared.

2. Aqueous acid hydrolyzes these compounds to the corresponding oximes; anhydrous hydrogen chloride converts aryl alkyl ketoxime-O-sulfonates to amides by a Beckmann-type rearrangement, and converts some dialkyl ketoxime-O-sulfonates to pyrazines in low yield.

3. These reactions are related to the direct reaction of hydroxylamine-O-sulfonic acid with ketones, and to the reactions of O-arylsulfonyl ketoximes.

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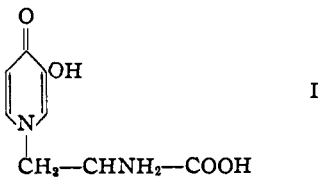
[CONTRIBUTION FROM THE DEPARTMENT OF RESEARCH IN PURE CHEMISTRY, MELLON INSTITUTE]

On the Structure of Leucaenine (Leucaenol) from *Leucaena Glauca* Bentham. III

BY A. F. BICKEL[1]

According to the experimental evidence now available, the most probable structure of leucaenine, an amino acid occurring in the tropical plant, *Leucaena glauca* Bentham, is β-[N-(3-hydroxypyridone-4)]-α-aminopropionic acid (I). The formation of 3,4-dihydroxypyridine on pyrolysis[2,3,4] and of N-methyl-3-methoxy-pyridone-4 on degradative methylation[5,6,7] proved the presence of a 3,4-dihydroxypyridine ring in leucaenine. These two reactions made it very probable that the part of the molecule containing the amino-acid residue is *not* bound to one of the carbon atoms of the pyridine ring. Since leucaenine is not split by treatment with 48% hydrobromic acid,[2] the alanine side-chain can*not* be bound to one of the hydroxyl groups of the ring. Hence, structure I was assumed to be the most probable.



I

The object of the present investigation was to attempt to provide definite proof of the existence of an alanine side-chain and to demonstrate its position in the molecule. It is known that a compound of a structure comparable to that of leucaenine, N-methyl-3-hydroxypyridone-4, yields methylamine[5] on oxidation with potassium permanganate. Should the oxidation of leucaenine proceed in the same way, formation of α,β-diaminopropionic acid may be expected. This diamino acid is, however, oxidized by potassium permanganate. Thus it was imperative to find an oxidizing agent capable of breaking the ring, while leaving the diamino acid unattacked. An aqueous solution of bromine proved to be a suitable reagent; hence the reaction of leucaenine with this oxidizing agent has been investigated more closely.

Upon oxidation of an aqueous suspension of leucaenine with bromine, a small amount of a compound $C_3H_9O_2N_2Br$ is formed. The specific rotation is $[\alpha]^{27}D$ +13° (33 mg. dissolved in 5 cc. of 0.37% hydrochloric acid). Aqueous solutions of this substance as well as of *dl*-α,β-diaminopropionic acid hydrobromide, prepared by synthesis, show an acid reaction (*p*H of the saturated solution in both cases, 4), react with an acidified aqueous solution of silver nitrate to yield silver bromide, and show a strong ninhydrin reaction. On heating in a melting point capillary, both compounds (as well as their mixture) gradually turn brown above 200° and melt above 236° with decomposition.

Geiger counter spectrometer diffraction patterns of the two substances were prepared with CuKα radiation. These patterns both show a large number of sharp diffraction lines, identical in positions and intensities in both cases.

Ultraviolet absorption spectra of aqueous solutions were found to be essentially the same for both compounds; they showed gradually increasing absorption with decreasing wave length, but no characteristic maxima.[8] The shape of the curves obtained closely resembles that found by Ley and Vanheiden[9] for *dl*-α,β-diaminopropionic acid hydrochloride.

The above facts clearly prove that the substance isolated is α,β-diaminopropionic acid hydrobro-

(1) Visiting Fellow, Netherland-America Foundation.

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

(3) Bickel, *ibid.*, 69, 1805 (1947).

(4) Adams, Jones and Johnson, *ibid.*, 69, 1810 (1947).

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

(6) Wibaut and Kleipool, *ibid.*, 66, 24 (1947).

(7) Bickel, THIS JOURNAL, 69, 1801 (1947).

(8) The author is indebted to Dr. Harold P. Klug, Dr. Alfred L. Marston and Mr. Joseph H. Lieblich, all of the Department of Research in Chemical Physics at Mellon Institute, for carrying out the physical determinations.

(9) Ley and Vanheiden, *Z. anorg. allgem. Chem.*, 188, 251 (1930).

mide; hence an alanine side-chain is bound to the nitrogen atom of the pyridine ring in leucaenine. This evidence establishes formula I as the correct structure for leucaenine.

The α,β-diaminopropionic acid *hydrochloride* showing a positive rotation is structurally related to the natural $l(-)$-serine.[10] Since the *hydrobromide* isolated also shows a positive rotation, it is very probable that leucaenine has the same stereochemical configuration as the other naturally-occurring amino acids. Natural leucaenine should therefore tentatively be designated as $l(-)$-leucaenine. (This result should be confirmed by comparison of the hydrochloride of the oxidation product with $l(+)$-α,β-diaminopropionic acid hydrochloride.)

Crystal structures of a racemic compound and of the corresponding *l*- and *d*-compounds are in general not the same; hence, one may expect a difference in melting points and X-ray diffraction patterns. The identity of these properties in the case of *dl*-α,β-diaminopropionic acid hydrobromide and the optically-active compound obtained on oxidation suggests, therefore, the absence of a racemic compound.

Another product obtained on oxidation of leucaenine by means of aqueous bromine solution is oxalic acid. It was isolated as the diammonium salt.

The optical rotation of leucaenine has been carefully re-determined and found to be $[\alpha]^{24}D$ $-22°$, in good accord with the value for mimosine given by Renz.[11]

With sulfuric acid, leucaenine forms a sulfate of the composition $C_8H_{10}O_4N_2 \cdot H_2SO_4 \cdot 1.5\ H_2O$.

Experimental

All melting points given are corrected.

α,β-Diaminopropionic Acid Hydrobromide. (A) From Leucaenine.—Leucaenine (2 g.) was suspended in 60 cc. of water, and bromine was added at room temperature until the color persisted (2.5 cc., or 5 moles of bromine per mole of leucaenine). After an hour the brown solution was evaporated *in vacuo* until the excess bromine had been removed, and then boiled with a great excess of lead carbonate until the evolution of carbon dioxide ceased. During this process the precipitate of lead bromide turned brown and a strong, aldehydic odor developed. After addition of Nuchar W, the reaction mixture was kept in the refrigerator overnight, and the lead bromide then filtered off and washed with ice-water. The yellow filtrate (*p*H 3) was treated with hydrogen sulfide, and the lead sulfide filtered off and washed with water. The final filtrate was evaporated *in vacuo* to dryness and the residue was dissolved in a small amount of water. After filtration, the brown solution was brought to *p*H 6 with 28% ammonia (0.5 cc.), again filtered, evaporated on the steam-bath until brown crystals separated, and filtered after cooling. One recrystallization from water (Nuchar W) gave colorless crystals which were dried in a vacuum desiccator over phosphorus pentoxide. Yield was 11 mg. (0.6%); m. p., above 236° with decomposition. In a second experiment the yield was 34 mg. (from 3 g. of leucaenine) or 1.2%.

Anal.[12] Calcd. for $C_3H_9O_2N_2Br$: C, 19.47; H, 4.90; N, 15.14; Br, 43.19. Found: C, 19.82; H, 4.64; N, 14.97; Br, 43.42.

(B) **From α,β-Dibromopropionic Acid.**—The preparation was carried out according to the directions of Winterstein.[13] Yield was 48%; m. p., above 236° with decomposition.

Anal. Calcd. for $C_3H_9O_2N_2Br$: C, 19.47; H, 4.90; N, 15.14; Br, 43.19. Found: C, 19.67; H, 4.71; N, 15.21; Br, 43.41.

A mixture of the hydrobromides from (A) and (B) melted above 236° with decomposition.

Ammonium Oxalate.—Leucaenine (1 g.) was dissolved in 5 cc. of 10% hydrobromic acid and bromine was added at room temperature until the color persisted. The excess bromine was removed *in vacuo* and the solution was evaporated in the vacuum desiccator over potassium hydroxide. The residue was dissolved in a small amount of water and the solution rendered neutral with 28% ammonia. On cooling, the needles which separated were filtered off, recrystallized once from water (Nuchar W), and dried at 110°. Yield was 50 mg.; m. p. 216–216.5° with decomposition.

Anal. Calcd. for $C_2H_8O_4N_2$: C, 19.36; H, 6.50; N, 22.58. Found: C, 19.71; H, 6.42; N, 22.78.

Ammonium oxalate prepared from oxalic acid and ammonia melted at 218–218.5° with decomposition; mixed melting point, 217.5–218° with decomposition.

Leucaenine Sulfate.—Leucaenine (0.99 g.) was dissolved in a warm solution of 0.52 g. of 95% sulfuric acid in 2 cc. of water. On cooling, the colorless crystals which separated were filtered off, and washed successively with water, ethanol, and ether. Yield was 1.53 g. (95%); m. p. 143–143.5°, with decomposition.

Anal. Calcd. for $C_8H_{10}O_4N_2 \cdot H_2SO_4 \cdot 1.5H_2O$: C, 29.70; H, 4.68; N, 8.67. Found: C, 29.49; H, 4.79; N, 8.68.

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Summary

A compound, $C_3H_9O_2N_2Br$, obtained on bromine oxidation of *leucaenine* has been proved to be α,β-diaminopropionic acid hydrobromide. This result establishes the structure of leucaenine as β-[N-(3-hydroxypyridone-4)]-α-aminopropionic acid.

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(10) See, among others, (a) Karrer, *Helv. Chim. Acta*, **6**, 411, 957 (1923); **9**, 301 (1926); (b) Schneider, *Ann.*, **529**, 1 (1937).

(11) Renz, *Z. physiol. Chem.*, **244**, 153 (1936).

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

(13) Winterstein, *Z. physiol. Chem.*, **59**, 146 (1909).