hydrochloride of ethylenediamine equivalent to 87% of the diamine originally used.

Anal. Calcd. for $C_2H_{10}N_2Cl_2$: N, 21.1. Found: N, 21.2.

2. In Alcohol Solution.—Alloxan anhydride (0.4 g. or 0.0028 mole) was dissolved in 15 cc. of absolute alcohol, and dry hydrogen chloride gas bubbled into the solution until it was decolorized to a pale yellow. After cooling in a refrigerator (two days) and finally filtering, 0.2 g. (0.0033 mole) of ethylenediamine in 10 cc. of absolute alcohol was added. A colorless, granular precipitate deposited, and took on a pink color on exposure to the air. It was separated, washed with absolute alcohol and ether and then dried *in vacuo* over concentrated sulfuric acid. The yield was only 0.5 g. The compound was free from chlorine. It was very soluble in water and attempts to purify it by precipitation from aqueous solution with acetone or pyridine, or by diluting an acetic acid solution with chloroform, were unsuccessful. A specimen dried to constant weight at 100° over phosphoric anhydride melted at about 214° with decomposition.

Anal. Calcd. for alloxan-[ethylenediamine-anilhydrate]-5, $C_6H_{10}O_4N_4$: C, 35.64; H, 4.9; N, 27.71. Found: C, 35.27, 36.2; H, 4.28, 4.53; N, 26.89, 28.1.

Two-tenths gram of the above condensation product was dissolved in 11 cc. of 0.1 *N* hydrochloric acid and combined with 22 cc. of water containing 0.3 g. of picric acid. After concentrating the solution *in vacuo*, and cooling, the picrate of ethylenediamine separated. This salt was purified by crystallization from water and melted at 227–235° with decomposition. When mixed with pure ethylenediamine picrate, no depression of the melting point was observed.

Anal. Calcd. for $C_{14}H_{14}O_{14}N_8$: N, 21.62. Found: N, 21.82.

Ethylenediamine gives an intense crimson coloration when added to an aqueous solution of alloxan. The dihydrochloride of the amine produces no coloration under the same experimental conditions. Furthermore, the presence of ethylenediamine dihydrochloride did not interfere with the formation of *alloxazine* by interaction of *o*-phenylenediamine dihydrochloride with alloxan in aqueous solution.

Interaction of *o*-Phenylenediamine Dihydrochloride with Methylalloxan-4-imino-5-oxime.—Toxoflavin and methylalloxan[12] react with *o*-phenylenediamine dihydrochloride in aqueous solution on warming to give methylalloxazine $C_{11}H_{18}O_2N_4$ (X). The above oxime derivative (IX)[13] does not interact with the *o*-diamine in a similar manner to form this alloxazine derivative. Combination in boiling water solution leads to the formation of an amorphous, brown substance which is soluble in hot acetic acid, and is reprecipitated in an amorphous condition by addition of water. We were unable to isolate any product of crystalline character from the reaction mixture.

Summary

1. Attention is called to the characteristic differences in chemical behavior of the pyrimidine alloxan toward aromatic and aliphatic amines.

2. Methylenediamine and alloxan do not interact to form xanthine or any tautomeric modification of this purine.

3. Ethylenediamine shows a different behavior toward alloxan than its aromatic analog *o*-phenylenediamine, and does not interact to form the corresponding aliphatic alloxazine analog. A simple addition product is formed without cyclization.

4. The oximido-imide (4,5) derivative of methylalloxan does not interact with *o*-phenylenediamine to form an alloxazine.

(12) VanVeen and Baars, *Rec. trav. chim.*, **57**, 259, 261 (1938).

(13) Traube, *Ber.*, **33**, 3048 (1900).

NEW HAVEN, CONN. RECEIVED JUNE 27, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

Synthesis of α-Aminopelargonic Acid

BY TREAT B. JOHNSON

At the urgent request of a group of workers in experimental medicine the author consented to undertake the synthesis of this unknown α-amino acid (I). Polypeptide combinations of this amino acid are believed to occur in the degradation products of the proteins of beet roots and in leaves of *Pelargonium roseum;* and several

$$CH_3CH_2CH_2CH_2CH_2CH_2CH_2CHCOOH$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad |$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad NH_2$$

I

dipeptide derivatives containing this amino acid have been described previously by Hopwood and Weizmann[1] in 1911.

The fact that pelargonic acid itself is known to influence certain physiological changes of interest to medicine, lends interest in the possible physiological behavior of the unknown amino acid and its derivatives. The fatty acid is characterized, for example, by its physical capacity as a surface-active substance and may act, depending upon the percentage present, as an accelerator or an

(1) Hopwood and Weizmann, *J. Chem. Soc.*, **99**, 1577 (1911).

TABLE I

Oenanthol, g.	Hydantoin, g.	Glac. acetic acid, cc.	Sod. acetate, g.	Time, hrs.	Temp., °C.	M. p., °C.	Hydantoin yield, g.
6	5	30	15	8	140–150	156–158	0.75
6	5	30	30	9	140–150	156–158	0.65
11.4	10	40	50	9	140–150	156–158	2.60
6	5	30	30	9	140–150	156–158	1.8
26	22.8	120	120	9	140–150	156–158	6.3
14	11.6	60	60	10	140–150	156–158	2.4

inhibitor of fermentation.[2] It also has been shown to be bactericidally effective toward certain organisms due to its marked surface-tension depressant action.[3] Addition of pelargonic acid to washed blood cells is known to increase their glucolytic activity to a marked degree. The acid exhibits also a characteristic physiological influence when incorporated into ester constructions of the procaine type (II). In the quantitative comparisons of a series of aliphatic procaine analogs it was shown that the narcotic effect of such esters increases in a normal series until the pelargonate derivative (II) is reached, when toxicity is enhanced to a maximum.[4]

$CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2COOCH_2CH_2N(C_2H_5)_2 \cdot HCl$

II

For the preparation of this amino acid (I) the author has applied successfully the aldehyde–hydantoin method of synthesis of α-amino acids originally developed in this Laboratory by Wheeler.[5] The different steps of this method are expressed below (III–VI).

$$\underset{\text{III}}{RCHO} \longrightarrow \underset{\text{IV}}{RCH{=}\overset{\displaystyle\frown}{C}CONHCONH} \longrightarrow$$

$$RCH_2\overset{\displaystyle\frown}{C}HCONHCONH \longrightarrow \underset{\text{V}}{RCH_2CHCOOH} \quad \underset{\text{VI}}{(NH_2)}$$

While this method of synthesis finds very general application when applied with aromatic aldehydes (R = C_6H_5, etc.), it has proved of no practical value, from a synthetic point of view, for the utilization of aliphatic aldehydes in α-amino acid synthesis. It is, therefore, of special interest to report that the author has succeeded in applying this technique of α-amino acid synthesis successfully with the aliphatic aldehyde—*oenanthol*. This aldehyde condenses with hydantoin to form the oenantholal-hydantoin (IV).[6] The latter compound is reduced easily to the saturated hydantoin (V); and this undergoes a normal hydrolysis by digestion with alkali yielding the desired α-aminopelargonic acid I.

(2) Windisch, Henneberg and Dietrich, *Biochem. Z.*, **107**, 172 (1920).

(3) Stanley and Adams, THIS JOURNAL, **54**, 1548 (1932).

(4) Brill and Bulow, *ibid.*, **55**, 2059 (1933).

(5) Wheeler and Hoffman, *Am. Chem. J.*, **45**, 368 (1911).

(6) R = $CH_3(CH_2)_5CH{=}$.

Experimental Part

Oenanthol, $CH_3(CH_2)_5CHO$.—*All* the oenanthol used in this work, with the exception of 10 g. of a Kahlbaum stock specimen, was manufactured by destructive distillation *in vacuo* of a high grade of castor oil. Heating this oil at an oil-bath temperature of 290–300° a fraction was collected which distilled from 60–68° at a pressure of 23–30 mm. This fraction of crude oenanthol was then purified by distillation at ordinary pressure and a fraction of oenanthol was finally collected boiling at 152–155°. Pure oenanthol boils at 155° at 760 mm. The average yield of oenanthol was 14 g. of the pure aldehyde from 280 g. of castor oil.

Condensation of Oenanthol with Hydantoin

Formation of $CH_3(CH_2)_5CH{=}C(CO{-}NH)(NH{-}CO)$, **Oenantholal-hydantoin.**—This hydantoin was obtained by digesting molecular proportions of hydantoin and oenanthol in glacial acetic acid solution with anhydrous sodium acetate. The results of the different condensations and the experimental conditions are recorded in Table I.

The yields of hydantoin condensation products were irregular and were not increased by incorporating acetic anhydride with the acetic acid and sodium acetate. After the end of the digestion period the reaction mixture was mixed with water and cooled. The unreacted oenanthol was extracted with ether, leaving behind the insoluble hydantoin derivative. This compound is purified easily by recrystallization from boiling absolute alcohol. It separates on cooling in the form of colorless rosets which melt at 157–159°.

Anal. Calcd. for $C_{10}H_{16}O_2N_2$: C, 61.22; H, 8.16; N, 14.28. Found: C, 61.01; H, 7.98; N, 14.31, 14.50.

The hydantoin dissolves easily in dilute sodium hydroxide solution and is reprecipitated by acidifying the alkaline solution with hydrochloric acid.

Reduction of Oenantholal-hydantoin

Formation of $CH_3(CH_2)_5CH(NH{-}CO)(CO{-}NH)$, **Hydantoin of α-Aminopelargonic Acid.**—For reduction of the above oenantholal-hydantoin the following reaction mixture was prepared: 5.5 g. of hydantoin, 12.5 g. of $SnCl_2 \cdot 2H_2O$, 75 cc. of 20% hydrochloric acid and 50 cc. of alcohol. This mixture was heated at boiling water-bath temperature for one and one-half hours and the excess of alcohol then

evaporated at 100°. The residue left behind was then triturated with water, filtered and the insoluble precipitate saved (see below). The aqueous filtrate was then saturated with hydrogen sulfide gas to precipitate tin as sulfide. After filtering off this tin sulfide precipitate and evaporating the filtrate to dryness no organic residue was recovered.

The insoluble precipitate (above) proved to be the desired reduction product. It was very insoluble in cold water, but separated from boiling water in colorless crystals melting at 142–143°. The total yield of pure crystallized hydantoin was 3.0 g. In a second experiment 8.8 g. of oenantholal-hydantoin was reduced under exactly the same conditions and yielded 8.8 g. of the desired reduced hydantoin.

Anal. Calcd. for $C_{10}H_{18}O_2N_2$: N, 14.14. Found: N, 14.17, 14.09.

Hydrolysis of the Reduced Hydantoin to α-Aminopelargonic Acid, $CH_3(CH_2)_6CH(NH_2)COOH$.—This hydantoin proved to be very resistant to hydrolysis by the action of barium hydroxide. Three grams of the pure reduced hydantoin was suspended in 1000 cc. of a hot, saturated solution of barium hydroxide and the mixture refluxed at its boiling point until the evolution of ammonia gas ceased. This actually required a digestion for fifty-six hours. The barium was then exactly precipitated as barium sulfate by adding the required amount of sulfuric acid, and bringing the solution to an exact neutral point to litmus. After filtering from barium sulfate, the clear aqueous solution was evaporated to dryness when we obtained 2.4 g. of the required α-aminopelargonic acid or 92.3% of the theoretical.

This α-amino acid is very difficultly soluble in hot water, alcohol, benzene and glacial acetic acid. It was purified for analysis by dissolving in hot, dilute hydrochloric acid, and cooling, when the hydrochloride of the amino acid crystallized out as fine colorless needles. This salt showed no definite melting point but slowly underwent decomposition on heating. It was dried for analysis over phosphorus pentoxide in an Abderhalden vacuum drier.

Anal. Calcd. for $C_9H_{20}O_2NCl$: N, 6.68; Cl, 16.94. Found: N, 6.90, 6.52; Cl, 16.81.

In order to obtain the free α-aminopelargonic acid (I) 1 g. of the above hydrochloride was dissolved in hot water and the solution allowed to cool slowly. The amino acid separated in the form of colorless, flaky crystals. This acid did not show a definite melting point and underwent decomposition when heated between 236 and 256°, giving off dense vapors. The yield of free acid was 0.63 g. The crystals gave no test for chlorine, indicating complete dissociation of the hydrochloride in aqueous solution.

Anal. Calcd. for $C_9H_{19}O_2N$: C, 62.42; H, 10.98; N, 8.10. Found: C, 62.23; H, 10.83; N, 8.40, 7.90.

Summary

1. Oenanthol can be utilized with success for the synthesis of α-aminopelargonic acid by application of the aldehyde-hydantoin method of amino acid synthesis.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, KWANGSI UNIVERSITY]

Synthesis of 2-*n*-Butyl-α-naphthol

BY YUOH-FONG CHI[1]

In this short paper is described a method of synthesizing 2-*n*-butyl-α-naphthol, which promises to have practical value as an antiseptic. This compound is formed by reducing 2-*n*-butyryl-α-naphthol, which is in turn obtained by condensing α-naphthol with *n*-butyric acid in the presence of fused zinc chloride.

It has long been known that fatty acids react in a characteristic manner with phenols and resorcinol in the presence of fused zinc chloride giving hydroxy-ketones.[2] α-Naphthol also condenses with glacial acetic acid in the presence of acetic anhydride and zinc chloride giving 2-acetyl-α-naphthol.[3] The author finds that α-naphthol reacts likewise with *n*-butyric acid giving 2-*n*-butyryl-α-naphthol, m. p. 85–86°, which is identified by formation of its oxime and semicarbazone. A secondary product of the reaction is α-naphthol *n*-butyrate.

The hydroxy-ketones, such as 2-acetylhydroquinone, 4-acetylresorcinol, 4-propionylresorcinol, 2-propionylhydroquinone, 4-*n*-butyrylresorcinol, 4-acetylanisole, 4-acetylphenetole, 4-propionylphenetole, 2,5-dimethoxypropiophenone, 3,4-dimethoxypropiophenone, etc., which contain the hydroxyl or alkoxyl group in the benzene ring, have been shown to undergo reduction to their corresponding alkyl derivatives by digesting with zinc amalgam and strong hydrochloric acid.[4] In like manneer 2-*n*-butyryl-α-naphthol is reduced

(1) The author desires to express here his appreciation of the help given by Professor Treat B. Johnson of Yale University in organizing this paper for publication.

(2) Nencki and Sieber, *J. prakt. Chem.*, [2] **23**, 147, 537 (1887); Nencki and Schmid, *ibid.*, **23**, 546 (1887); Goldsweig and Kaiser, *ibid.*, [2] **43**, 86 (1891); Crepieux, *Bull. soc. chim.*, [3] **6**, 151 (1891); Nencki, *Ber.*, **26**, R587 (1893); Dzierzgowski, *ibid.*, **26**, R588 (1893); Pauly and Lockemann, *ibid.*, **48**, 30 (1915); Johnson and Lane, THIS JOURNAL, **43**, 348 (1921); Dohme, Cox and Miller, *ibid.*, **48**, 1688 (1926).

(3) Witt and Braun, *Ber.*, **47**, 3219 (1914).

(4) Clemmensen, *ibid.*, **47**, 54 (1914); Johnson and Hodge, THIS JOURNAL, **35**, 1014 (1913); Johnson and Lane, *ibid.*, **43**, 348 (1921); Sonn, *Ber.*, **54**, 773 (1921).