

Anal. Calcd. for $C_6H_8O_2N_2S$: C, 37.50; H, 5.03. Found: C, 37.83; H, 5.05.

Oxidation of Homocysteine Hydantoin.—Fifty mg. of homocysteine hydantoin was titrated with 2.9 cc. of 0.1 *N* iodine solution which is 93% of the theoretical. The crystals which precipitated were collected by filtration, dried and gave a m. p. of 201–203°. A mixed m. p. with homocysteine hydantoin gave no depression.

Oxidation of Cysteine Hydantoin.—Sixty-four and a half mg. of cysteine hydantoin consumed 4.4 cc. of 0.1 *N* iodine solution which is the theoretical quantity. The crystals were collected on a filter and dried. The com-

pound decomposed above 300° and gave a positive disulfide test.

Summary

1. The preparation of the hydantoins of *l*-cysteine, *dl*-homocysteine, *S*-benzylhomocysteine, and *dl*-homocystine has been described.

2. The hydantoin ring is stable to the reduction of sodium in liquid ammonia.

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RECEIVED JANUARY 6, 1944

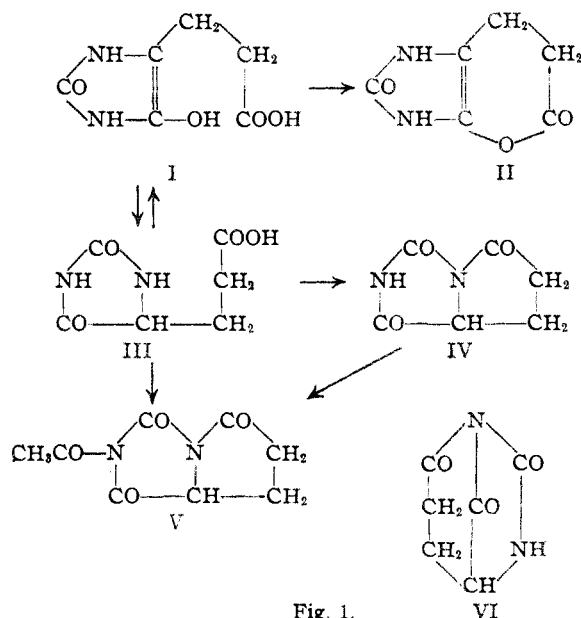
[CONTRIBUTION FROM THE RESEARCH LABORATORIES, S. M. A. CORPORATION]

The Dehydration of Hydantoin-5-propionic Acid

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Introduction

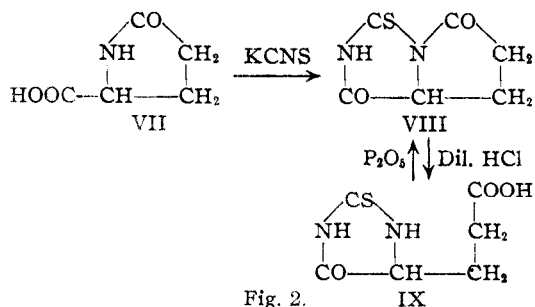
If it is assumed that hydantoins may enolize, three possible structures (II, IV and VI) may be postulated for the compound obtained by the dehydration of hydantoin-5-propionic acid. Dakin¹ has stated that such an enolization ($III \rightleftharpoons I$) is possible since racemization of optically active hydantoins probably occurs through this mechanism.



By the action of phosphoric anhydride on hydantoin-5-propionic acid (III) a molecule of water was split out and the resulting product obtained in good yield. Theoretically this could be either II, IV or VI. Acetylation of the acid as well as the lactam yielded the same mono-acetyl derivative (V). Neither the dehydration product nor the acetyl derivative reacted with aqueous potassium permanganate or bromine in carbon tetra-

chloride. The mono-acetyl derivative could not be acetylated further under conditions which yielded diacetyl hydantoin. These facts tend to indicate one of the lactam formulas (IV or VI).

However, the structure of the dehydration product was shown by the following experiment. 2-Thiohydantoin-5-propionolactam-1 (VIII) had been synthesized previously from pyrrolidone carboxylic acid and ammonium or potassium thiocyanate by Johnson and Guest² and also by Nicolet and Johnson.³ By desulfurization of the thiohydantoin with chloroacetic acid they obtained hydantoin-5-propionic acid instead of hydantoin-5-propionolactam-1. Hydrolysis with dilute hydrochloric acid gave 2-thiohydantoin-5-propionic acid (IX). It was obvious, therefore, that if the acid (IX) could be converted back to the lactam (VIII) by dehydration with phosphoric anhydride, we could assume that hydantoin-5-propionic acid undergoes a similar reaction and that our dehydration product is the oxygen analog of VIII, *i. e.*, hydantoin-5-propionolactam-1 (IV). 2-Thiohy-



antoin-5-propionic acid (IX) was obtained by the hydrolysis of VIII and converted back to VIII by dehydration with phosphoric anhydride. We may assume, therefore, that the dehydration of hydantoin-5-propionic acid yields hydantoin-5-propionolactam-1 (IV) and not hydantoin-5-propionolactam-3 (VI) or the lactone (II).

(1) Dakin, *Am. Chem. J.*, **44**, 48 (1910).

(2) Johnson and Guest, *ibid.*, **47**, 242 (1912).

(3) Nicolet and Johnson, *ibid.*, **49**, 204 (1913).

Experimental

dl-Hydantoin-5-propionic Acid (III).—Hydantoin-5-propionic acid was prepared in a 62% yield from sodium glutamate and potassium cyanate according to the directions of Dakin.¹ After recrystallization from water, the product melted at 170°.⁴

Hydantoin-5-propiolactam-1 (IV).—Hydantoin-5-propionic acid (1.7 g.) was refluxed for two hours in 15 cc. of xylene containing 0.5 g. of phosphorus pentoxide. The mixture was allowed to stand overnight and crystals separated. The solvent was decanted and the crystals washed with 10 cc. of cold methanol and then recrystallized from 70% methanol. The yield was 1.2 g. (78%) of product melting at 196–198°. After three recrystallizations the substance melted sharply at 201°.

Anal. Calcd. for C₈H₁₀O₃N₂: C, 46.75; H, 3.92; N, 18.18. Found: C, 46.87; H, 4.12; N, 18.25.

1-Acetyl-hydantoin-5-propiolactam-1 (V).—A mixture of hydantoin-5-propionic acid (5 g.) and acetic anhydride (25 cc.) was refluxed for one hour. The excess solvent was removed by distillation *in vacuo* and the residue was crystallized by the addition of alcohol. Recrystallization from alcohol yielded 5 g. (88%) of product melting at 147–148°. One gram of this product was refluxed for four hours with acetic anhydride and recovered unchanged.

Anal. Calcd. for C₉H₁₀O₄N₂: C, 48.98; H, 4.11. Found: C, 48.96; H, 4.31.

Acetylation of Hydantoin-5-propiolactam-1.—Twenty-five mg. of hydantoin-5-propiolactam-1 was acetylated under the same conditions as the hydantoin-5-propionic acid and yielded a product melting at 147–148°. A mixed

(4) All melting points were recorded on a micro stage and are uncorrected.

melting point with the product obtained by the acetylation of hydantoin-5-propionic acid showed no depression.

2-Thiohydantoin-5-propiolactam-1 (VIII).—Pyrrolidone carboxylic acid (VII) (40 g.) (from glutamic acid) and 28 g. of ammonium thiocyanate were warmed on a steam-bath with 180 cc. of acetic anhydride and 20 cc. of glacial acetic acid. A red solution was obtained which yielded 22 g. (43%) of crystals (m. p. 206–207°) after the addition of benzene. The recorded m. p. is 206–207°.

2-Thiohydantoin-5-propionic Acid (IX).—Two grams of (VIII) was refluxed with 25 cc. of 1 *N* hydrochloric acid for one-half hour and cooled. Two grams (90%) of acid (IX) melting at 121.5–122° crystallized out. The recorded m. p. is 122°.

Dehydration of 2-Thiohydantoin-5-propionic Acid (IX).—Two hundred mg. of IX was refluxed for two hours with 15 cc. of toluene containing 100 mg. of phosphorus pentoxide. The solvent was decanted while hot from a small amount of brown residue. On cooling crystals separated from the toluene solution. The yield was 120 mg. (66%) melting at 206–207°. A mixed m. p. with the lactam (VIII) gave no depression.

Acknowledgment.—We wish to thank Mr. John M. Kolbas for his assistance in the preparation of the manuscript.

Summary

The products obtained by the dehydration and the acetylation of hydantoin-5-propionic acid have been shown to possess the lactam structure IV and V.

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RECEIVED JANUARY 6, 1944

NOTES

Synthesis of Bromoacetals

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Of the many syntheses of bromoacetal reported, that of Filachione¹ is the most convenient. It consists of slow addition of bromine to a mixture of vinyl acetate and alcohol at very low temperature (–40°). A recent modification of this method² involves very slow addition (ten hours) of bromine in the vapor form to a well-cooled mixture of vinyl acetate and alcohol.

The yields in both procedures are not high, being 46% for dimethyl acetal and 58–68% for diethyl acetal, and the method is rather cumbersome and time-consuming. Its chief disadvantage appeared to be the presence of methyl or ethyl alcohol during the bromination reaction, necessitating slow addition of bromine at low temperatures in order to prevent the bromination of the alcohol.

When bromine is added to a mixture of vinyl acetate and carbon tetrachloride at 0–10°, addition is very rapid and in the theoretical quantities. On adding the mixture to methyl or ethyl alcohol

(99.5–100%) with cooling, a rapid reaction takes place with the formation of bromoacetal. This method is applicable to small or large scale preparations and the yields are of the order of 80–85% for dimethyl acetal and 75–80% for diethyl acetal.

Contrary to previous reports, bromoacetal freed from traces of bromoacetaldehyde by means of bisulfite or fractionation is not a lachrymator but does possess a rather pungent odor. On standing for several weeks a slight decomposition takes place with the formation of bromoacetaldehyde.

Experimental

Preparation of Bromoacetaldehyde Dimethyl Acetal.—One mole of vinyl acetate (86 g.) b. p. 71–73° was added to 150 ml. of carbon tetrachloride and cooled in an ice-water mixture. A mixture of 90 ml. of carbon tetrachloride and 160 g. of bromine was added to the vinyl acetate mixture with shaking, care being taken not to allow the temperature to rise above 10°. The addition took about twenty minutes and the end-point was reached when bromine no longer decolorized. The brominated mixture was then added to 350 ml. of methyl alcohol (99.5–100%), and cooled during the first hour to prevent rise in temperature as bromoacetal is formed. It was shaken occasionally and allowed to stand for two days. The mixture which consisted of two layers was diluted with one liter of water and the bromoacetal-carbon tetrachloride layer drawn off. The methyl alcohol-water mixture was further ex-

(1) Filachione, *THIS JOURNAL*, **61**, 1705 (1939).

(2) "Organic Syntheses," **28**, 8 (1943).