0.2 mm. and was somewhat unstable.[7] The substance was identified as a decahydroheptalene dione (or a mixture of isomers) by formation of two derivatives.

The di-2,4-dinitrophenylhydrazone, for which no solvent for recrystallization was found, was purified by washing with hot methanol, hot water and hot methanol; m.p. 125–126°.

Anal. Calcd. for $C_{24}H_{24}N_8O_8$: C, 52.17; H, 4.35; N, 20.28. Found: C, 52.42; H, 4.84; N, 19.94.

The disemicarbazone, for which no satisfactory solvent could be found, was purified by successive washing with hot methanol, hot water and hot methanol. It had no discernible melting point but decomposed above 250°.

Anal. Calcd. for $C_{14}H_{24}N_6O_2$: C, 54.54; H, 7.79; N, 27.27. Found: C, 54.76; H, 7.79; N, 26.93.

(7) Other ketonic compounds in this series have been observed to be unstable. See G. Buchi and O. Jeger, *Helv. Chim. Acta*, **32**, 538 (1949).

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The Hydantoin Derivative of 4-Thiazolidinecarboxylic Acid

BY MARVIN D. ARMSTRONG[1]

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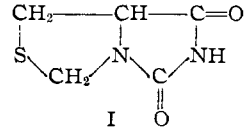
The hydantoin derivative of 4-thiazolidinecarboxylic acid (I) is of interest as a new derivative of cysteine and as an example of a fused ring system analogous to that of some hydantoins and thiohydantoins prepared during the studies of the chemistry of penicillin.[2] Both the D- and L-forms of the hydantoin have been prepared by causing the corresponding thiazolidinecarboxylic acids to react with potassium cyanate and then treating the reaction mixture with acid. Neither isomer showed penicillin activity when assayed with *B. subtilis*, nor biotin activity for *S. cerevisiae*.



I

Experimental

L-4-Thiazolidinecarboxylic acid was prepared according to the procedure of Schubert.[3] To a suspension of 0.50 g. of this compound in 25 ml. of water was added 0.61 g. of potassium cyanate; all of the thiazolidinecarboxylic acid went into solution. The solution was heated on a steam-bath for 30 minutes, then acidified by the addition of concd. HCl, an additional 0.5 ml. of concd. HCl was added, and the solution was evaporated to a low volume on a steam-bath. The solid that crystallized when the solution was cooled was collected and recrystallized from a small volume of water; yield 0.41 g. (69%), m.p. 167°. The compound is soluble in dil. alkali, slightly soluble in water and insoluble in acids, alcohol or acetone. It gives a negative test for sulfhydryl when treated with sodium nitroprusside, both before and after treatment with sodium cyanide.

When the rotation is measured immediately upon dissolving in 1 *N* NaOH, $[\alpha]^{20}D$ −115° (*c* 1); the rotation gradually decreases over a period of 12 hours, and then remains constant at $[\alpha]^{20}D$ −23°.

Anal. Calcd. for $C_5H_6O_2N_2S$: C, 37.98; H, 3.80; N, 17.72; S, 20.25. Found: C, 38.06; H, 4.21; N, 17.61; S, 20.53.

The corresponding derivative prepared from D-cysteine hydrochloride was identical with the above compound in all its chemical and physical properties with the exception of the optical rotation; for a 1% solution in 1 *N* NaOH, $[\alpha]^{20}D$ +115°, decreasing to $[\alpha]^{20}D$ +23°.

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(1) Univ. of Utah College of Medicine, Salt Lake City, Utah.

(2) "The Chemistry of Penicillin," Princeton University Press, 1949, pp. 302, 970, 971.

(3) M. P. Schubert, *J. Biol. Chem.*, **114**, 341 (1936).

Experimental Chemotherapy of Tuberculosis. IV. 2-Piperazinecarboxylic Acid and Related Compounds

BY F. L. BACH, JR., S. KUSHNER AND J. H. WILLIAMS

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In view of the high antituberculous activity of Aldinamide,[1a] pyrazinamide,[1b] it was considered necessary to investigate the effect of various changes in the chemical constitution of this compound. One variation of interest was the reduced form of pyrazinamide, namely, 2-piperazinecarboxamide. Since pyrazine derivatives of this type are not easily reduced, 2-piperazinecarboxylic acid, a new acid, was synthesized as an intermediate.

The disodio derivative of N,N′-di-*p*-tosylethylenediamine was condensed with ethyl α,β-dibromopropionate in a refluxing ethanolic potassium hydroxide solution to yield the ethyl ester of 1,4-di-*p*-tosyl-2-piperazinecarboxylic acid. Hydrolysis of the ester and detosylation occurred when this derivative was refluxed in 48% hydrobromic acid. The free acid released by silver carbonate in an aqueous medium was very soluble in water, insoluble in the ordinary organic solvents and was characterized as a white, crystalline solid which melted with decomposition at 275–277°. The infrared spectrum of this substance shows a typical amino acid carboxylate ion absorption at 6.32 μ.[2] Attempts to esterify 2-piperazinecarboxylic acid by the usual methods such as refluxing with ethanol and hydrogen chloride or by treatment with diazomethane were unsuccessful. However, esterification can be accomplished by a prolonged refluxing of the acid in ethanol, benzene and concentrated sulfuric acid, followed by a periodic distillation from the reaction of an azeotropic mixture consisting of ethanol, benzene and water. The ester prepared in this manner was treated with hydrazine hydrate (100%) to yield 2-piperazinecarboxylic acid hydrazide and an ammonolysis of ethyl 2-piperazinecarboxylate afforded the desired product, 2-piperazinecarboxamide.

The 2-piperazinecarboxylic acid which was purified by sublimation *in vacuo* gave an elemental analysis and neutralization equivalent in accord with the calculated amounts and an electrometric titration of the dihydrochloride of this acid showed end-points at *p*H 3.7, 7.5 and 10.6. One molar equivalent of this cyclic amino acid when condensed with two molar equivalents of ninhydrin in a warm, neutral, aqueous solution gives a deep-red colored solution. A similar reaction between proline and

(1) (a) The trade-mark of American Cyanamid Company for pyrazinamide is Aldinamide; (b) S. Kushner, H. Dalalian, J. L. Sanjurjo, F. L. Bach, Jr., S. R. Safir, V. K. Smith, Jr., and J. H. Williams, THIS JOURNAL, **74**, 3617 (1952).

(2) H. M. Randall, R. G. Fowler, N. Fuson and J. R. Dangl, "Infrared Determination of Organic Structures," D. Van Nostrand Co., Inc., New York, N. Y., 1949, p. 16.