are such that both can be explained by further oxidations of the formaldehyde resulting from the 1,2-glycol-cleaving reaction and no rearrangement of an intermediate or oxidation–reduction exchange between reaction products need be postulated. The periodate system is the more suitable of the two reagents studied for carrying out degradations in carbon tracer studies of the origin of the glycerol residue in physiologically important materials structurally related to glycerol.

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β-(2-Thienyl)-serine

BY MATTHEW E. DULLAGHAN AND F. F. NORD

The preparation of β-phenylserine by the condensation of benzaldehyde and glycine has been reported by Erlenmeyer.[1,2] In the course of studies on the chemistry of heterocyclics,[3] initiated in this Laboratory,[4] it became necessary to have available α-amino-β-hydroxy-β-(2-thienyl)-propionic acid, *i.e.*, β-(2-thienyl)-serine.

Experimental

A mixture of 2-thenaldehyde (0.5 mole),[3] glycine (0.25 mole) and 100 ml. of absolute ethanol was, therefore cooled to 3° in an ice-bath. A cold solution of potassium hydroxide (0.5 mole) in 150 ml. of absolute ethanol was added with stirring at such a rate that the temperature of the mixture remained below 10°. After all the alkali had been added, and a white precipitate started to form, the mixture was allowed to remain below 10° overnight to enable maximum precipitation. Upon filtration of precipitate, it was washed with absolute ethanol, then dissolved in water (75 ml.) and the solution acidified with 15 ml. of glacial acetic acid. Ethanol (75 ml.) was added and the mixture again allowed to stand in an ice-bath at 5° for two hours. The resulting solid upon filtration was recrystallized from 50% water–ethanol. The yield of white needles amounted to 19 g. (41%). The substance started to soften and turned brown at 185–186°, melting at 194–195° (uncor.) under decomposition.

Anal. Calcd. for $C_7H_9NO_3S \cdot H_2O$: C, 40.97; H, 5.36; N, 6.87. Found: C, 41.13; H, 5.29; N, 6.80.

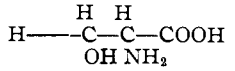
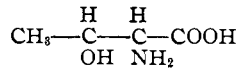
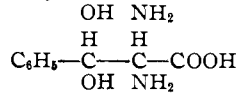
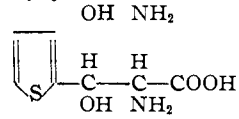
It is presumed that the β-(2-thienyl)-serine so obtained belongs to the DL-threose series. This belief is based on the fact that this was shown to be the case with phenylserine.

Discussion

While the amino acid is named as an analog of serine, it could also be considered as one of threonine. Since β-(2-thienyl)-alanine is a known antagonist for β-phenylalanine, the series of analogous amino acids listed in Chart I indicate interesting possibilities in further studies of this type.

Even though serine is not an essential amino acid in that it can be synthesized by the animal from glycine, it is possible that the now available β-(2-thienyl)-serine could act as a competitor for serine in protein synthesis, leading to a serine deficiency. Too, penicillamine is thought to act as a competitor for the decarboxylase converting serine to amino ethanol causing a choline deficiency.[5] β-(2-Thienyl)-serine because of its similarity to both penicillamine and serine could act in a similar manner.

CHART I

Serine	
Threonine	
Phenylserine	
β-(2-Thienyl)-serine	

(1) Erlenmeyer, *Ber.*, **25**, 3445 (1892).

(2) Erlenmeyer and Früstück, *Ann.*, **284**, 36 (1895).

(3) King and Nord, *J. Org. Chem.*, **13**, 635 (1948); Dullaghan and Nord, Abstracts of the 119th Meeting of the Am. Chem. Soc., 34M (1951).

(4) This work was carried out under the aegis of the Office of Naval Research.

(5) Wilson and du Vigneaud, *J. Biol. Chem.*, **184**, 63 (1950).

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The Synthesis of Compounds for the Chemotherapy of Tuberculosis. II. Hydroxamic Acid Derivatives

BY THOMAS S. GARDNER, E. WENIS AND F. A. SMITH

In the course of the preparation of pyridine derivatives[1] for testing as anti-tubercular agents, nicotinohydroxamic acid was prepared. This was found to be inactive. Shortly afterwards, Urbánski[2] reported tuberculostatic activity of salicylhydroxamic acid in mice and, on these grounds, we prepared further members of the pyridine hydroxamic acid series, namely, picolinohydroxamic acid, isonicotinohydroxamic acid, 3-pyridineacetohydroxamic acid and 5-cyano-6-hydroxy-2-methylisonicotinohydroxamic acid. As a representative of another heterocyclic system, 5-methyl-3-isoxazolecarbohydroxamic acid was made. For control purposes salicylhydroxamic acid was prepared according to Jeanrenaud,[3] and on the ground of the tuberculostatic activity of *p*-aminosalicylic acid, *p*-aminosalicylhydroxamic acid was also made. None of these compounds, including the salicylhydroxamic acid, displayed any anti-tubercular activity in a mouse prophylactic test in which nicotinamide, *p*-aminosalicylic acid, thiosemicarbazones[1] and streptomycin showed activity.

Acknowledgment.—We are grateful to Drs. R. J. Schnitzer and E. Grunberg of our Chemotherapy Laboratories for testing the compounds and to Dr. A. Steyermark and his associates for the microchemical analyses.

Experimental

The method described in the first preparation was employed in all cases (Table I) except that the hydrochloride was not prepared when the hydroxamic acid crystallized.

4-Amino-2-hydroxybenzohydroxamic Acid Hydrochloride.—A solution of sodium methylate was prepared by treating 12 g. of sodium with 300 ml. of anhydrous methanol. To this was added 35 g. of hydroxylamine hydrochloride, and after 30 minutes of stirring, 36 g. (0.215 mole) of methyl *p*-aminosalicylate was added. The reaction mixture was stirred at 25° for 16 hours and filtered. The filtrate was evaporated to dryness and the residue extracted with boil-

(1) T. S. Gardner, F. A. Smith, E. Wenis and J. Lee, *J. Org. Chem.*, 6, 1121 (1951).

(2) T. Urbánski, *Nature*, **166**, 267 (1950).

(3) A. Jeanrenaud, *Ber.*, **22**, 1270 (1889).