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.

DEPARTMENT OF CHEMISTRY
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RECEIVED MAY 14, 1951

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.

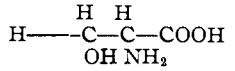
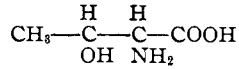
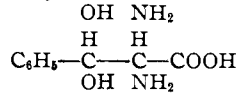
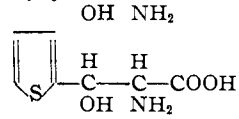
It is presumed that the β-(2-thienyl)-serine so obtained belongs to the DL-threose series. This belief is based on the fact that this was shown to be the case with phenylserine.

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).

COMMUNICATION NO. 233 FROM THE DEPARTMENT OF ORGANIC CHEMISTRY AND ENZYMOLOGY
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RECEIVED JUNE 13, 1951

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).

TABLE I

Hydroxamic acid	Formula	M.p., °C.	Yield, %	Nitrogen, % Calcd.	Found
Picolino-	$C_6H_6O_2N_2$·HCl	190–191	46	16.1	16.3
Nicotino-[a]	$C_6H_6O_2N_2$·HCl	186–187	49	16.1	15.9
Isonicotino-	$C_6H_6O_2N_2$·HCl	206–207	70	16.1	15.8
3-Pyridineaceto-[b]	$C_7H_8O_2N_2$	177–178	73	18.4	18.5
5-Cyano-6-hydroxy-2-methyl-isonicotino-	$C_8H_7O_3N_3$	>250	65	[c]	
5-Methyl-3-isox-azolecarbo-	$C_5H_6O_3N_2$	143–145	56	19.7	19.2

[a] The free base has been reported without being characterized. E. Frommel, A. Bischler, I. T. Beck, F. Vallette and M. Favre, *Inter. Z. Vitaminforsch.*, 19, 193 (1947). [b] The free base was crystallized from ethanol. [c] The product was obtained as a yellow powder by triturating with hot water and then with hot glacial acetic acid. *Anal.* Calcd.: C, 49.8; H, 3.6. Found: C, 50.0; H, 4.1.

ing ethanol (500 ml.). The filtered ethanolic extracts were treated with hydrogen chloride gas, and the product which separated was dissolved in a minimum quantity of hot water; on addition of ethanol and cooling, crystallization of the acid salt occurred; yield 26 g. (59%), m.p. 237°.

Anal. Calcd. for $C_7H_8O_3N_2$·HCl: N, 13.7. Found: N, 13.2.

RESEARCH LABORATORIES OF HOFFMANN-LA ROCHE, INC.
NUTLEY 10, N. J. RECEIVED MAY 11, 1951

The Diffusion Coefficients of Sodium and Potassium Iodides in Aqueous Solution at 25°[1]

By P. J. DUNLOP[2] AND R. H. STOKES

In earlier papers[3] are reported measurements of the diffusion coefficients of eight uni-univalent chlorides and bromides. The present note deals with similar studies of sodium and potassium iodides.

Experimental.—The general technique of the measurements, which employ magnetically-stirred porous-diaphragm cells, has already been described.[3] Potassium iodide was the British Drug Houses "Analar" product, used without further purification. Sodium iodide was the same maker's laboratory reagent grade; gravimetric analysis of the thoroughly dried salt for iodide indicated a purity of 99.5%. As the most probable impurities are other sodium salts of very similar diffusion coefficients, no further purification was considered necessary. The cells were calibrated at frequent intervals by diffusing 0.1 *N* KCl into water, using the measurements of Harned and Nuttall as standards, as previously explained.[3]

Table I presents the integral diffusion coefficients $\bar{D}^0$ (after correction to refer to runs of zero duration) for various values of the average concentration c_m' on the lower (more concentrated) side of the diaphragm. In Table II the integral and differential diffusion coefficients are listed at round concentrations obtained by the methods listed.[3]

In connection with a theoretical interpretation of the results for the ten uni-univalent electrolytes so far studied, values of the relative viscosities of the solutions are required. Since the available data for sodium iodide[4] are somewhat sparse and are not given at 25°, they were supplemented by the measurements given in Table III. These were made with an Ostwald viscometer of standard pattern having a flow-time of 623 sec. for air-free water at 25°. Its accuracy was checked by meas-

(1) This note summarizes a thesis submitted by P. J. Dunlop in partial fulfillment of the requirements of the degree of Bachelor of Science with Honors in the University of Western Australia.

(2) Chemistry Department, University of Wisconsin.

(3) R. H. Stokes, THIS JOURNAL, **72**, 763, 2243 (1950).

(4) "International Critical Tables," Vol. V, p. 15.

TABLE I

INTEGRAL DIFFUSION COEFFICIENTS AT 25°

$\bar{D}^0(c_m')$ = integral diffusion coefficient corrected to zero duration of run (cm.^{2} sec.$^{-1}$ × 10^{-5}). c_m' = mean of initial and final concentrations on lower side of diaphragm (moles/liter).

Sodium iodide		Potassium iodide	
c_m'	$\bar{D}^0(c_m')$	c_m'	$\bar{D}^0(c_m')$
0.04193	1.554	0.04263	1.932
.04396	1.549	.04383	1.927
.08608	1.535	.08339	1.907
.08811	1.539	.08401	1.906
.08916	1.535	.09213	1.904
.09011	1.538	.09340	1.904
.09073	1.535	.1673	1.883
.09181	1.537	.1748	1.882
.1729	1.529	.1783	1.883
.1759	1.533	.2624	1.879
.2697	1.534	.2753	1.874
.2740	1.534	.3670	1.881
.3743	1.534	.4404	1.890
.3874	1.539	.6090	1.909
.4434	1.541	.6157	1.910
.6142	1.560	.8856	1.940
.6237	1.559	.9079	1.940
.9235	1.579	1.485	2.010
.9324	1.571	1.487	2.006
1.412	1.614	1.936	2.050
1.425	1.612	1.970	2.052
1.675	1.641	2.471	2.101
1.982	1.668	2.494	2.104
1.998	1.667	2.561	2.112
2.341	1.701	3.072	2.161
2.364	1.701	3.100	2.167
2.801	1.742	3.899	2.225
2.835	1.739		
3.439	1.785		

TABLE II

INTEGRAL AND DIFFERENTIAL DIFFUSION COEFFICIENTS AT ROUND CONCENTRATIONS

D = differential diffusion coefficient (cm.^{2} sec.$^{-1}$ × 10^{-5}). $\bar{D}^0 = \frac{1}{c}\int_0^c D\,dc$ = integral diffusion coefficient for experiments of vanishingly short duration between concentration c and pure water. c = moles solute/liter.

c	$\bar{D}^0$ (NaI)	$\bar{D}^0$ (KI)	D (NaI)	D (KI)
0.0[a]	1.616	2.001	1.616	2.001
.05	1.549	1.923	1.527	1.891
.1	1.536	1.900	1.520	1.865
.2	1.530	1.879	1.532	1.859
.3	1.534	1.876	1.547	1.884
.5	1.546	1.896	1.580	1.955
.7	1.559	1.919	1.612	2.001
1.0	1.582	1.953	1.662	2.065
1.5	1.623	2.008	1.751	2.166
2.0	1.667	2.058	1.846	2.254
2.5	1.711	2.107	1.925	2.347
3.0	1.753	2.154	1.992	2.440
3.5		2.203		2.533

[a] Nernst limiting values.

TABLE III

RELATIVE VISCOSITIES OF SODIUM IODIDE SOLUTIONS AT 25°

η = viscosity of solution. η^0 = viscosity of water. c = moles NaI/liter.

c	0.290	0.607	1.050	2.059	2.947
η/η^0	1.008	1.015	1.032	1.094	1.201