TABLE II

AMINO ANILINO ALKANOLS

Compound (R′ = aminoanilino)	Cryst. from	M. p., °C.	Molecular formula	Nitrogen, % Calcd.	Found
2-(4-Chloro-2-R′)-ethanol	C_6H_6	122.5	$C_8H_{11}ON_2Cl$	15.01	15.17
3-(4-Chloro-2-R′)-propanol-2	C_6H_6	130	$C_9H_{13}ON_2Cl$	13.96	13.99
3-(4-Chloro-2-R′)-2-methylpropanol-2	C_6H_6	121	$C_{10}H_{15}ON_2Cl$	13.06	13.01
2-(4-Chloro-2-R′)-2,2-dimethyl ethanol	C_6H_6–pet. ether		$C_{10}H_{15}ON_2Cl$	13.06	12.94
2-(5-Chloro-2-R′)-ethanol	$C_6H_5CH_3$	104.5	$C_8H_{11}ON_2Cl$	15.01	15.00
3-(5-Chloro-2-R′)-propanol-1	C_6H_6–pet. ether	73.5	$C_9H_{13}ON_2Cl$	13.96	13.87
3-(5-Chloro-2-R′)-propanol-2	C_6H_6–pet. ether	101.5	$C_9H_{13}ON_2Cl$	13.96	14.00
2-(3-Chloro-2-R′)-ethanol	$C_6H_5CH_3$	74	$C_8H_{11}ON_2Cl$	15.01	14.88
2-(6-Chloro-2-R′)-ethanol	Oil	135–137 (2 mm.) (b. p.)	$C_8H_{11}ON_2Cl$	15.01	15.06

pared from 3,5-dichloroacetanilide.[3] The former boiled at 100–101° (4 mm.); the latter at 105–107° (3 mm.).

Condensations.—The appropriate dichloronitrobenzene was dissolved in butanol and twice the molar quantity of the desired amino alcohol added. The mixture was then refluxed for approximately four hours. Upon cooling the reaction mixture in ice, the condensation product frequently was found to separate as a highly colored solid. In some instances, steam distillation of the reaction mixture was resorted to whereupon the condensation product separated out in the steam distillation flask upon cooling.

(3) Holleman and De Mooy, *Rec. trav. chim.*, **35**, 1 (1916).

Reduction of the nitro compounds was effected with sodium hydrosulfite in a weakly alkaline medium.

In the case of the 2,4-dichloronitrobenzene condensation, the position of the hydroxy alkyl group was established by effecting the condensation using 3,4-dinitrochlorobenzene. Identical products were obtained. Hence the mobile chlorine atom in the 2,4-dichloronitrobenzene is that ortho to the nitro group.

Summary

A number of new chloronitroanilino and chloroaminoanilino alkanols, intermediates of pentryl analogs, are reported.

NEW YORK, N. Y. RECEIVED JANUARY 30, 1942

[CONTRIBUTION FROM THE LABORATORY OF THE BURNHAM SOLUBLE IODINE COMPANY]

Bis(Amino Acid) Derivatives. I. Diglycine[1] Halogen Acid Addition Products

BY WALTER S. FROST

Attempts to prepare crystalline glycine hydriodide from a glycine–water solution treated with excess hydriodic acid proved unsatisfactory. When, however, two molecules of glycine were used with one of hydriodic acid a white crystalline product with a sharp melting point and the theoretical iodine content for diglycine hydriodide was obtained. Further investigation showed that other diglycine acid addition products may be easily prepared.

The diglycine hydrochloride,[2] diglycine nitrate[3] and diglycine picrate[4] have been reported previously.

(1) Refers to two glycine molecules, not glycylglycine.

(2) K. Kraut and F. Hartmann, *Ann.*, **133**, 101 (1865).

(3) (a) M. V. Dessaignes, *Ann. chim. phys.*, III, **34**, 143 (1852); *Ann.*, **82**, 236 (1852); (b) J. V. Dubský and J. Maitner, *Práce Mor. Přírodověd. spol. v Brně*, **6**, No. 3; *Chem. Obzor*, **10**, Abstract sect., 45 (1935); see *C. A.*, **30**, 7478 (1936).

(4) P. A. Levene and D. D. Van Slyke, *J. Biol. Chem.*, **12**, 285 (1912).

Experimental

Diglycine Hydrochloride.—This compound can be made in several ways. When theoretical quantities of glycine and monoglycine hydrochloride or theoretical quantities of glycine and hydrochloric acid are brought together in water the diglycine compound can be recovered either by cooling the hot saturated solution or by evaporation. It may also be made by cooling a hot saturated solution of glycine with excess monoglycine hydrochloride or excess hydrochloric acid in water or by cooling a hot saturated solution of monoglycine hydrochloride or hydrochloric acid and excess glycine in glacial acetic acid.

For instance, using equivalent quantities in water, 22.3 g. of monoglycine hydrochloride (calcd. for $C_2H_6ClNO_2$: Cl, 31.79. Found: Cl, 31.78, m. p. 176–177°) and 15 g. of glycine were dissolved in 30 cc. of water on heating nearly to boiling. The colorless crystals formed on cooling, ground and dried, weighed 24 g. (64% yield); m. p. 186–187°.

Anal. Calcd. for $C_4H_{11}ClN_2O_4$: Cl, 19.00; N, 15.01. Found: Cl, 19.01; N, 14.91; mol. wt. (Rast), impossible because of insolubility.

Using excess glycine in glacial acetic acid, 4.46 g. of monoglycine hydrochloride and 4.52 g. of glycine (150%) were dissolved in 400 cc. of boiling glacial acetic acid under a reflux condenser. The copious fine white precipitate formed on cooling was washed several times with acetic acid; yield 7.04 g. (94%); m. p. 187°.

Anal. Calcd. for $C_4H_{11}ClN_2O_4$: Cl, 19.00. Found: Cl, 18.91.

Monoglycine Hydrobromide.—Fifteen grams of glycine was treated with 33.1 cc. of hydrobromic acid containing 24.3 g. of hydrogen bromide (150%). All dissolved on warming. After evaporation the light brown crystals were ground and further dried, becoming nearly colorless; m. p. 143–144°. The compound is hygroscopic.

Anal. Calcd. for $C_2H_6BrNO_2$: Br, 51.23. Found: Br, 51.31.

Diglycine Hydrobromide.—Made by evaporation of water solutions of glycine and monoglycine hydrobromide and glycine and hydrobromic acid in theoretical quantities; m. p. 163–165° (av.).

Anal. Calcd. for $C_4H_{11}BrN_2O_4$: Br, 34.59. Found: Br, 34.44 (av.).

Diglycine Hydriodide.—This compound was prepared by crystallization from hot solutions of glycine in both water and acetic acid containing excess hydriodic acid; m. p. 169–170° (av.).

Anal. Calcd. for $C_4H_{11}IN_2O_4$: I, 45.64. Found: I, 45.82 (av.).

Discussion

The diglycine hydrochloric, hydrobromic and hydriodic acid compounds are colorless crystals, stable in the dry condition. They yield the free halogen acids on dissolving in water. They are very soluble in water but the first two are less soluble than the corresponding monoglycine compounds. Their water solubility increases with rise in atomic weight of the halogen. They are insoluble in alcohol and ether. Attempts to prepare the corresponding hydrofluoric acid compounds were not successful.

Information on the structure must await investigation. The possibilities of the use of the diglycine compounds in glycine separations and identification are of interest as well as their usefulness as therapeutic agents. It would seem to be desirable to determine which types of the following compounds $(CR_2NR_2COOH)_2 \cdot HX$ can exist where R refers to H or various organic radicals. Compounds in which the amino group is on other than the alpha carbon atom also should be investigated. The dialanine compounds are under investigation and other reports are contemplated.

Summary

Methods for the preparation of the diglycine derivatives of hydrochloric, hydrobromic and hydriodic acids and the compounds themselves have been described. Possibilities for further research have been suggested.

AUBURNDALE, MASSACHUSETTS
RECEIVED JANUARY 29, 1942

[CONTRIBUTION FROM THE COLLEGE OF PHARMACY, UNIVERSITY OF CALIFORNIA]

Sulfophenylarsonic Acids and Certain of Their Derivatives. VI. Derivatives of *p*-Sulfonamidophenylarsonic Acid.[1]

BY E. L. WAY AND J. F. ONETO

In continuation of our problem relative to studies of sulfophenylarsonic acids and certain of their derivatives, we have extended the number of sulfonamide derivatives of *p*-sulfonamidophenylarsonic acid as indicated in Tables I and II. A number of these compounds are being prepared in quantity for toxicological and pharmacological investigations, the results of which will be published elsewhere.

The condensation of benzylaniline, *p*-aminobiphenyl, morpholine and piperidine with *p*-chlorosulfonylphenylarsonic acid was carried out in aqueous media according to a method described in a previous publication.[2] Condensation of methylaniline with the above-mentioned sulfonyl chloride was effected by a procedure previously employed in the preparation of *p*-arsono-N-phenylbenzenesulfonamide.[3] The diiodoarsines and arsine oxides appearing in Tables I and II were prepared in the usual way with hydriodic acid and ammonium hydroxide. The oxides were obtained as arsenoso or arsonoso derivatives depending upon the conditions of isolation and purification. *p*-Arsenoso-N-methyl-N-phenylbenzenesulfonamide, for example, was obtained upon precipita-

(1) Aided by a grant from John Wyeth and Brother.

(2) Oneto and Way, THIS JOURNAL, **63**, 762 (1941).

(3) Oneto and Way, *ibid.*, **61**, 2106 (1939).