duced pressure, to one-half its original volume and then cooled in a refrigerator for twelve hours. Thirty grams of α-chlorodiphenylacetyl chloride, melting at 48.5–49.5°, is obtained. Further concentration of the mother liquor yields a second crop of crystals weighing 15–25 g.; yield, 65–80%.

Preparation of N,N'-Substituted α-Aminodiphenylacetamides.—To 0.06 mole of α-chlorodiphenylacetyl chloride, dissolved in about 75 ml. of dry ether, 0.12 mole of an amine is added slowly with shaking. Ammonia, methylamine and ethylamine are added by bubbling the gas through the solution kept at 0°. The reaction mixture is allowed to stand at room temperature for three to five hours and is then filtered to remove the amine hydrochloride. The ether solution is concentrated to 25 ml., placed in a pressure bottle and 0.12 mole of amine added. After sealing the bottle the reaction mixture is maintained at 50–60° for several days. The contents are filtered and the filtrate extracted three times with 15-ml. portions of dilute hydrochloric acid. In order to extract the diphenetidine derivative it is necessary to use concentrated hydrochloric acid. The combined acid washings are almost neutralized with solid sodium carbonate and brought to neutrality with a saturated solution of the carbonate. The neutral solution is boiled gently to remove excess amine. When the odor of amine is no longer detectable, the solution is decanted and the remaining, solid or liquid, substituted α-aminodiphenylacetamide is purified by dissolving in about 25 ml. of boiling methyl alcohol and diluting with hot water until a faintly turbid solution results.

Summary

1. A modified procedure has been described for the preparation of α-chlorodiphenylacetyl chloride.

2. A number of substituted derivatives of α-aminodiphenylacetamide have been prepared. Pharmacological tests show that some of these compounds possess both anticonvulsant and antispasmodic activity.

BLOOMINGTON, INDIANA RECEIVED JANUARY 28, 1943

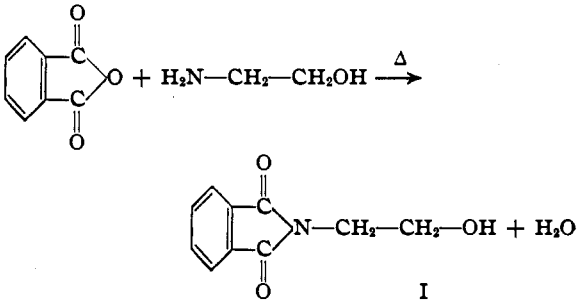
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF INDIANA UNIVERSITY]

Amino Acids. I. Glycine

BY JOHN H. BILLMAN AND EARL E. PARKER

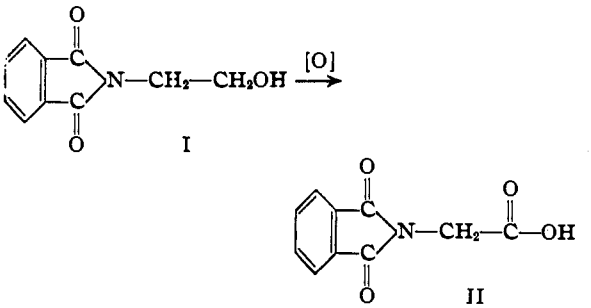
The customary methods used for the synthesis of glycine are the amination of a halogenated acetic acid or the hydrolysis of aminoacetonitrile formed from methyleneaminoacetonitrile.[1]

A new method for the synthesis of glycine has been developed which involves the reaction of ethanolamine and phthalic anhydride to produce β-hydroxyethylphthalimide (I) in a 99% yield.[2]

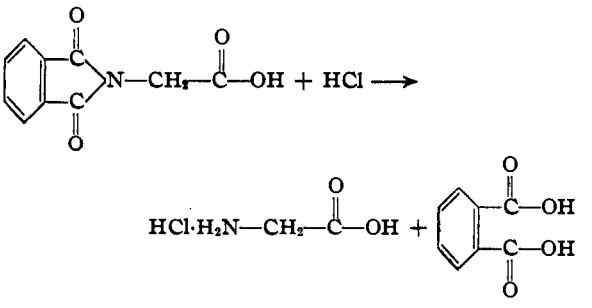


A study of the oxidation of β-hydroxyethylphthalimide (I) to phthalylglycine (II) was made and found to give an 89–93% yield of crude material when acidified potassium dichromate was used as the oxidizing agent.

It was unnecessary to purify the phthalylglycine which was readily hydrolyzed by refluxing



with 18% hydrochloric acid solution for ten hours. The phthalic acid formed by hydrolysis of (II) was removed by filtering the reaction mixture after cooling in an ice-water bath. Upon evaporation of the filtrate glycine hydrochloride was obtained.



The over-all yield of glycine hydrochloride from ethanolamine was 79–85%.

(1) "Organic Syntheses," Coll. Vol. I, 1941, pp. 298–301

(2) Wenker. THIS JOURNAL, 59, 422 (1937).

By the use of the pyridine and alcohol method glycine was obtained from the glycine hydrochloride in a 65–73% yield.

This method of synthesis is being extended to the preparation of numerous other amino acids.

We wish to thank Eli Lilly and Company for assistance in this work.

Experimental

β-Hydroxyethylphthalimide.—In a 1-liter Erlenmeyer flask fitted with a variable take-off condenser was placed 148 g. of phthalic anhydride. To this was added 61 g. of pure ethanolamine at such a rate that the reaction did not become too vigorous. The reaction mixture was then heated to 175° and kept at that temperature for two hours at the end of which time 18 cc. of water had been removed at the take-off. The melt was cooled and recrystallized out of 500 cc. of water. A yield of 181 g. melting at 126–127° was obtained. An additional 8 g. of pure material was obtained by evaporating the filtrate to 50 cc. The total yield was 189 g. or 99%.

Phthalylglycine.—In a 2-liter three-neck flask fitted with a dropping funnel and a stirrer, was placed 25 g. of β-hydroxyethylphthalylimide, 800 cc. of water containing 30.1 g. of potassium dichromate and 10 cc. of glacial acetic acid. A solution of 25.5 g. of sulfuric acid and 250 cc. of water was added to the above mixture over a period of fifteen minutes during which time the solution was being heated to boiling. After the solution had boiled for one-half hour the flame was removed and the mixture was allowed to cool overnight. The next day the phthalylglycine was filtered off, washed with cold water to remove the chromium salts, and the combined filtrates placed in a two-liter flask. The solution was concentrated under reduced pressure to about 450 cc., cooled to 5°, filtered and washed. The total weight of phthalylglycine separated at this point was about 20 g. Upon further concentration to about 200 cc. a precipitate was obtained which was contaminated with a considerable amount of chromium salts. This mixture along with the material obtained by further evaporation to 50 cc. was dried and extracted with acetone. The acetone solution was evaporated to dryness and yielded an additional 4 to 5 g. of phthalylglycine free from chromium compounds. This made a total of 24.0–24.8 g. of crude product; yield 89–93%. Attempts at this point to purify the phthalylglycine took considerable time and caused some loss of the phthalyl compound. Since the only impurity at this point is phthalic acid which is removed in the next step it is advisable to use the crude material for the following hydrolysis.

Glycine Hydrochloride.—To 24.8 g. of the impure phthalylglycine in a 500-cc. ground-glass jointed flask, fitted with a reflux condenser, was added 250 cc. of 18% hydrochloric acid and the mixture refluxed vigorously for ten hours. The solution was then cooled to 5° and filtered to remove the phthalic acid. The filtrate was then evaporated to dryness under reduced pressure. Two 20-cc. portions of water were added to the flask and the mixture evaporated to dryness, under reduced pressure, after each addition. The process was then repeated three more times using 15 cc. of absolute alcohol in place of the water; yield 11.6–12.6 g. or 79–85% based on ethanolamine. Purified phthalglycine gives a 98% yield.

Glycine.—To 10 g. of glycine hydrochloride was added 10 cc. of water and the mixture was warmed until the glycine hydrochloride dissolved. At this point 10 cc. of pyridine was added and the glycine was precipitated by the addition of 50 cc. of methyl alcohol. The mixture was allowed to cool for four hours in the refrigerator. The glycine was then filtered off and washed with three or four 20-cc. portions of methyl alcohol to free it of pyridine. Glycine obtained by this method was free of halogen and weighed 4.4–4.9 g.; yield 65–73%.

Summary

1. Glycine hydrochloride has been prepared in a 79–85% yield by a new method.

2. Glycine has been obtained from glycine hydrochloride in a 65–73% yield.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Condensation of Amino Alcohols with Benzene

BY C. M. SUTER AND A. WAYNE RUDDY[1]

The condensation of simple alcohols with benzene in the presence of aluminum chloride has been described in the literature[2] but no report has been found of such a condensation when the alcohol molecule also contains an amino group. In the present study of the behavior of a variety of amino alcohols with benzene it has been shown that in the presence of a considerable excess of anhydrous aluminum chloride a tertiary amino alcohol such as 1-amino-2-methyl-2-propanol gives a high yield of the β,β-dialkylphenethylamine.

$$C_6H_6 + (CH_3)_2C(OH)CH_2NH_2 \xrightarrow{AlCl_3} C_6H_5C(CH_3)_2CH_2NH_2 + H_2O$$

On the other hand 1-amino-2-propanol reacts to only a slight extent and no reaction occurs with ethanolamine. The condensation takes place with the amino alcohols containing a

(1) Sharp and Dohme post-doctorate Fellow, 1940–1941.

(2) Huston and Kaye, THIS JOURNAL, 64, 1576 (1942). This reference reviews much earlier work.