

of diazomethane. Methyl streptobiosaminidic acid has been further characterized by the preparation of the amide and its tetraacetate. BRUNSWICK, N. J. RECEIVED SEPTEMBER 3, 1946

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## An Improved Synthesis of *dl*-Lysine

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The von Braun synthesis of *dl*-lysine,<sup>1</sup> which has been improved recently by Eck and Marvel,<sup>2</sup> presents one of the most satisfactory ways of preparing this amino-acid. The key intermediate in this synthesis is  $\epsilon$ -aminocaproic acid. This is benzoylated, the benzoyl derivative converted with phosphorus and bromine to the  $\alpha$ -bromo acid and the latter ammonolyzed and finally hydrolyzed to *dl*-lysine.

We have simplified this method by using sulfur chloride in the halogenation of  $\epsilon$ -benzoylaminocaproic acid and proceeding *via* the  $\alpha$ -chloro acid. In contrast to phosphorus and bromine, which produce a violent exothermic reaction and form mixtures of such a consistency that efficient stirring is impossible, sulfur chloride reacts at moderate temperatures, mildly, non-exothermically and forms a homogeneous solution. Moreover, the yields with phosphorus and bromine are erratic and vary between 60 and 90%, whereas sulfur chloride consistently gives yields of 96–98%. Finally, the use of sulfur chloride is by far more economical than that of bromine of which considerable amounts are required in the von Braun synthesis.

These improvements, together with the fact that  $\epsilon$ -caprolactam and  $\epsilon$ -aminocaproic acid have recently become commercially available, render the preparation of large amounts of *dl*-lysine convenient and economical.<sup>3</sup>

### Experimental

**$\epsilon$ -Benzoylamino-caproic Acid.**—Sixty-seven and eight-tenths g. (0.6 mole) of  $\epsilon$ -caprolactam, 48 g. (1.2 mole) of sodium hydroxide and 300 ml. of water were refluxed for thirty minutes.<sup>4</sup> The mixture was cooled in an ice-bath and 86.5 g. (0.62 mole) of benzoyl chloride was added dropwise with stirring and keeping the temperature at 20°. When the addition was finished, the mixture was stirred

for an additional fifteen minutes. It was then diluted to 1500 ml. with water and made acid by the addition of an excess of hydrochloric acid (1;1). The acid must be added slowly at the beginning, otherwise the material may precipitate as an oil or in large lumps. Seeding and cooling helps to obtain it in fine crystals. The mixture is allowed to stand in an ice-bath for two and one-half hours whereupon the crystals were filtered off, washed  $\text{Cl}^-$  free and dried at 40–50°; yield, 132 g. (93.5%), m. p. 75–78°.

**$\epsilon$ -Benzoylamino- $\alpha$ -chlorocaproic Acid.**—Thirty-five and three-tenths grams (0.15 mole) of  $\epsilon$ -benzoylaminocaproic acid and 0.5 g. of finely powdered iodine were dissolved in 70 ml. of sulfur chloride and heated under reflux in a water-bath at 60–65°. There was a copious evolution of gas which slowed down after one to one and one-half hours. During the next one and one-half hours the bath was gradually brought to the boiling point and the reaction was complete. The excess sulfur chloride was removed by distillation and the residue shaken with 120 ml. of water, decanted and washed with two portions of hot water, 120 ml. each. The crude chloro-acid is a pale yellow solid which was dried *in vacuo* and weighed 38.7–39.32 g. (96–97.5%), m. p. 115–125°. It was used directly, without further purification, in the next step. A small additional amount of material crystallized out from the mother liquors used in the washing of the crude acid.

Pure  $\epsilon$ -benzoylamino- $\alpha$ -chlorocaproic acid obtained by recrystallization from a very dilute aqueous solution melted at 145–147° and had a neutral equivalent of 268–269 (theory, 269.5).

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_{16}\text{O}_3\text{NCl}$ : C, 57.9; H, 5.94; N, 5.2; Cl, 13.17. Found: C, 57.5; H, 6.0; N, 5.3; Cl, 12.9.

***dl*- $\epsilon$ -Benzoyllysine.**—Two and two-tenths grams of crude chloro-acid was dissolved in 40 ml. of concentrated ammonia and heated in a pressure-bottle for seven and one-half hours at 85–90°. The mixture was then evaporated *in vacuo* to dryness, the residue taken up in a small amount of water, filtered, washed with water followed by methanol and dried; yield 1.30 g. (60% of  $\epsilon$ -benzoylaminocaproic acid), m. p. 265–270° (dec.).

*dl*- $\epsilon$ -Benzoyllysine was converted to *dl*-lysine hydrochlorides according to the procedures described in the literature.<sup>1,2</sup>

### Summary

An economical and convenient procedure for the preparation of *dl*-lysine is described. It consists in converting  $\epsilon$ -caprolactam or  $\epsilon$ -aminocaproic acid to  $\epsilon$ -benzoylaminocaproic acid, chlorinating the latter with sulfur chloride in the presence of iodine, ammonolyzing the resulting  $\alpha$ -chloro acid and hydrolyzing to *dl*-lysine.

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(1) von Braun, *Ber.*, **42**, 839 (1909).

(2) Eck and Marvel, *J. Biol. Chem.*, **106**, 387 (1934); "Organic Syntheses," Coll. Vol. 2, John Wiley and Sons, New York N. Y., 1943.

(3)  $\epsilon$ -Caprolactam and  $\epsilon$ -aminocaproic acid are available from E. I. du Pont de Nemours & Co., Inc.; sulfur chloride from Hooker Electrochemical Company.

(4) When an equivalent amount of  $\epsilon$ -aminocaproic acid is used, this step, of course, is not necessary.