

## PDF hosted at the Radboud Repository of the Radboud University Nijmegen

The following full text is a publisher's version.

For additional information about this publication click this link.

<http://hdl.handle.net/2066/143005>

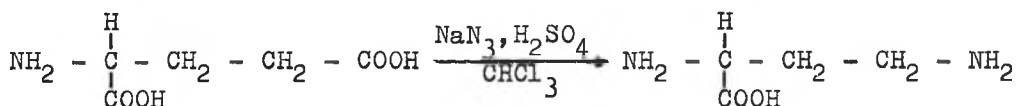
Please be advised that this information was generated on 2018-07-07 and may be subject to change.

NOTE ON THE PREPARATION OF L- $\alpha,\gamma$ -DIAMINO BUTYRIC ACID

G.I. Tesser and J.W. van Nispen

Department of Organic Chemistry, R.C. University, Nijmegen  
The Netherlands

In our laboratory we needed L- $\alpha,\gamma$ -diaminobutyric acid and we successfully tried to improve the method of Adamson (1) (scheme 1). As there are many articles in the literature dealing with the synthesis of this compound (sometimes making use of tedious isolation procedures and leading to yields ranging from 15 to 62% (2-8)), it appeared useful to describe our method.



(scheme 1)

Our improvement had two aspects. First, the Schmidt reaction as applied by Adamson, could be brought very near to completion by very efficient mixing of the reactants. For that purpose we used a conical reaction flask (of 370 ml) with a wide ground joint (B55), equipped with a three way adaptor holding a reflux condenser, a stirring rod of a very efficient stirring apparatus (Vibro-Mischer, model E1 from "A.G. für Chemie-Apparatenbau", Switzerland, plunger diameter of 45 mm, 17 mm apart from the walls of the vessel) and a stopper.

In the flask 100 mmol of L-glutamic acid (=14.72 g) and 70 ml sulfuric acid (about 100%) were placed. After dissolution effected by stirring and gentle heating, 70 ml chloroform were added, followed by one equivalent of sodium azide (=6.50 g) in one portion. The temperature raised within a few seconds till the boiling point of chloroform and was maintained between 50 and 62°C during the course of the reaction. After one, four and six hours another equivalent of sodium azide was added. After eight hours only a trace of glutamic acid was left (a very faint spot with Rf 0,65 remained; EtOH-H<sub>2</sub>O (7 : 3); silica). However, we found a faint, ninhydrine-positive spot on the chromatogram with an Rf-value of 0,31 (Dab : 0,10, in the same system). After isolation of the crude product, the impurity could be removed by crystallization.

The second aspect of the improvement concerned the working up of the reaction mixture: an ion exchanger was used for the separation of the product from the huge amount of sulfuric acid. After cooling to room temperature, the reaction mixture was poured into enough distilled water to obtain a half molar sulfuric acid solution and, after separating from the chloroform layer, this solution was filtered slowly during the night through a column of Dowex 50 X 2 (dry mesh 200-400) (diameter of the column 58 mm, length 72 cm, filled with 700 ml wet Dowex). The capacity of the ion exchanger was 0.80 meq/ml resin.

The filtrate appeared completely free of diaminobutyric acid and was discarded. The column was washed free from sulfuric acid with distilled water (until the pH of the effluent was about 5) and the product eluted with 4 M ammonia. The filtrate was evaporated to dryness, the residue dissolved in water, treated with charcoal, and taken to dryness again. The solid was dissolved in a small amount of hydrochloric acid (4 N), the pH adjusted to 5 with pyridine and the product precipitated with 96% ethanol. The L- $\alpha$ , $\gamma$ -diaminobutyric acid monohydrochloride, thus obtained in 90% yield (=13.90 g) was chromatographically pure and analysed correctly for C<sub>4</sub>H<sub>10</sub>N<sub>2</sub>O<sub>2</sub>.HCl; m.p. 226-227°C

[lit.: 225° (5,7,8)];  $[\alpha]_D^{28} = +22.5 \pm 1^\circ$  (c=1, 6 N HCl)

[lit.:  $[\alpha]_D^{20} = +25.3 \pm 0.5^\circ$  (c=1.1, 5 N HCl) (5);

$[\alpha]_D^{21} = +23.8^\circ$  (c=1.2, 6 N HCl) (7) and  $[\alpha]_D^{15} = +22.0 \pm 0.4^\circ$   
(c=4.4, 5 N HCl) (8)].

## References:

- 1) D.W. Adamson, J.Chem.Soc., 1939, 1564.
- 2) For a survey see J.P. Greenstein and M. Winitz in the "Chemistry of the amino acids", Vol.3, p.2469, J. Wiley, New York, 1961.
- 3) I.K. Mushakwar and R.E. Koeppe, J.Biol.Chem., 238, 2460 (1963).
- 4) M. Zaoral, Coll.Czech.Chem.Comm., 24, 1314 (1959).
- 5) M. Zaoral and J. Rudinger, *ibid.*, 24, 1993 (1959).
- 6) M. Martha Pigretti and A.O.M. Stoppani, Anales Assoc.Quim. Arg., 49, 55; 161 (1961).
- 7) S. Wilkinson, J.Chem.Soc., 1951, 104.
- 8) H. Kawasaki, Nippon Kagaku Zasshi, 81, 280 (1960); C.A. 55, 6393i (1961).

Received: August 3, 1971