



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

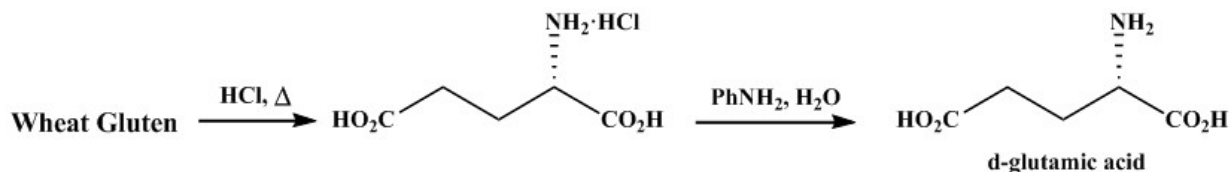
In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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d-GLUTAMIC ACID



Submitted by Harold King

Checked by H. T. Clarke and S. Gurin.

1. Procedure

(A) *Glutamic Acid Hydrochloride*.—A mixture of 300 cc. of concentrated hydrochloric acid and 100 g. (corrected for moisture) of gluten flour is boiled under reflux for six hours. When the solution has cooled to room temperature it is treated with 20 g. of decolorizing carbon and filtered by suction through two thicknesses of linen covered with a thin layer of infusorial earth; 15 cc. of concentrated hydrochloric acid is employed for rinsing the flask and washing the residue. The light yellow filtrate is concentrated under reduced pressure to 175 cc. (Note 1) and allowed to stand overnight at -8° . The crystals which separate, amounting to 25–26 g., are filtered off on hardened paper. The mother liquor is further concentrated to 75 cc. and again allowed to stand overnight at -8° . A second crop amounting to 16–18 g. is thus obtained. Further concentration yields no more crystals.

The crude product, which is yellow in color, is dissolved in 40 cc. of hot water, decolorized with 1 g. of charcoal, and treated with 33 cc. of concentrated hydrochloric acid. After standing overnight in the refrigerator, the first crop, weighing about 23 g., is obtained. This melts with decomposition at $208\text{--}209^\circ$ (corr.). On concentrating the mother liquors two further crops of equal purity can be obtained, giving a total yield (Note 2) of 26–27 g. of glutamic acid hydrochloride of satisfactory quality.

(B) *Glutamic Acid*.—To a solution of 36.7 g. (0.2 mole) of pure glutamic acid hydrochloride in 200 cc. of hot water is added 18.6 g. (0.2 mole) of aniline. The mixture, after heating for a few minutes on the steam bath, is cooled, treated with 200 cc. of 95 per cent ethyl alcohol, and allowed to stand overnight in the refrigerator. The crystalline glutamic acid is filtered off and washed with 95 per cent ethyl alcohol until free of chloride. It is then pure, and melts with decomposition at $211\text{--}213^\circ$ (corr.). The yield (Note 3) and (Note 4) is 27–28 g. (92–95 per cent of the theoretical amount).

2. Notes

- In checking this preparation no crystals were obtained on chilling the original unconcentrated filtrate to -8° and holding it at this temperature for seventy-two hours.
- The yield will depend in a large measure on the quality of the gluten flour; that employed for checking (Battle Creek Gluten flour) contained 8.7 per cent moisture, and 7.4 per cent nitrogen on the dry basis.
- The glutamic acid so obtained is of high quality, which cannot be improved by recrystallization from water. In fact such recrystallization is attended with loss owing to the formation of pyrrolidone-carboxylic acid. The mother liquor yields no further crystals on concentration under reduced pressure to 75 cc. and treatment with 75 cc. of alcohol.
- Glutamic acid may also be obtained from "Ajinomoto,"¹ a Japanese food product in powder form, consisting mainly of the monosodium salt of glutamic acid. The exact amount of this constituent may be determined by the Van Slyke amino nitrogen method and by igniting a sample of the material in a platinum crucible and titrating the residue of sodium carbonate. The calculated quantity of normal hydrochloric acid is added to a solution of the Ajinomoto in four times its weight of water, and then the solution is boiled with a little decolorizing carbon and filtered hot; the clear solution is allowed to stand overnight in the ice box and the crystallized glutamic acid is filtered and washed with ice water. In this way, 72–73 per cent of the theoretical amount can be obtained; thus, 100 g. of Ajinomoto, found to

contain 84 g. of **monosodium glutamate**, was dissolved in 400 cc. of water and treated with 500 cc. of normal **hydrochloric acid**, when 54–55 g. of pure **glutamic acid** was obtained.

3. Discussion

d-Glutamic acid hydrochloride can be prepared by the hydrolysis of gliadin from wheat,² casein,³ and technical residues like beet-sugar molasses⁴ or alcohol-extracted soybean cake.⁵ The acid has been synthesized from **acrolein** through β -aldehydobutyric acid,⁶ and by the alkylation of benzoylaminomalonic ester with β -bromopropionic ester followed by hydrolysis.⁷

d-Glutamic acid can be prepared from the hydrochloride by treating a water solution with strong alkalis,³ alkali carbonates,⁸ aqueous ammonia,⁹ aniline,¹⁰ and by adding 6–8 volumes of alcohol to a concentrated aqueous solution.¹¹

The preparation of *d*-glutamic acid from Ajinomoto¹² is very convenient, but more expensive than that from flour.

References and Notes

1. Ajinomoto may be obtained from S. Suzuki and Co., New York City.
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10. Anslow and King, Biochem. J. **21**, 1171 (1927).
11. Hopkins, *ibid.* **15**, 293 (1921).
12. Schmidt and Foster, Proc. Soc. Exptl. Biol. Med. **18**, 205 (1921).

Appendix

Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

benzoylaminomalonic ester

β -aldehydobutyric acid

β -bromopropionic ester

ethyl alcohol,
alcohol (64-17-5)

hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

aniline (62-53-3)

Acrolein (107-02-8)

sodium carbonate (497-19-8)

nitrogen (7727-37-9)

decolorizing carbon (7782-42-5)

Glutamic Acid Hydrochloride (138-15-8)

Glutamic Acid (56-86-0)

pyrrolidone-carboxylic acid

monosodium salt of glutamic acid,
monosodium glutamate