The Synthesis of L-*Theanine*

By Toshiyuki FURUYAMA, Takeshi YAMASHITA and Saburo SENOH

(Received February 15, 1964)

In the course of investigations of flavor substances in Japanese green tea, Sakato discovered L-glutamic acid γ-ethyl amide in the water extract and named theanine.[1] The synthesis of this substance has since been reported by several authors.[2-8] Sakato et al.,[3] for instance, synthesized it from *N*-carbobenzoxy-L-glutamic acid γ-ethyl ester, and Hashizume[4] and Tsuchiya et al.,[8] from pyrrolidonecarboxylic acid.

The synthesis described here is based on the reaction between amino groups of amino acids and carbon disulfide in the presence of alkali, giving dithiocarbamates and protecting the amino group.[9] The procedure is as follows: In the solution of 10 ml. of ethanol and 2 ml. of carbon disulfide, 4 g. of γ-methyl L-glutamate was dispersed. To the mixture, 50 ml. of anhydrous ethylamine*1 was added under cooling with ice-water. The solution was left to stand for ten days at room temperature in a sealed flask. The excess ethylamine, carbon disulfide and ethanol were then distilled off in vacuo. The residual oily material was suspended in 25 ml. of 5 N acetic acid and heated for 30 min. at 60°C under reduced pressure. The carbon disulfide which had protected the amino group of the product was split off by this procedure. The residual solution was concentrated to some extent, and ethanol added. L-Theanine crystallized out in a yield of 1 g. Recrystallization from water-ethanol afforded L-theanine (m.p. 215°C with decomp.) and $[\alpha]_D^{18}$ +8.7° (*c* 1.743, water).*2

Found: C, 48.11; H, 8.06; N, 16.01. Calcd. for $C_7H_{14}O_3N_2$: C, 48.26; H, 8.10; N, 16.08%.

The favorable protection of the amino group with carbon disulfide gave L-theanine without any racemization. Boissonnas previously synthesized optically-pure L-glutamine by protecting the amino group by carbon disulfide.[10] When his scheme was used, scarcely any formation of pyrrolidonecarboxylic acid occured. The present reaction appears to proceed in a manner analogous to Boissonnas' scheme.

Technical Research Laboratory
Asahi Chemical Industry Co., Ltd.
Itabashi-ku, Tokyo

1) Y. Sakato, *J. Agr. Chem. Soc. Japan* (*Nippon Nogei Kagaku Kaishi*), **23**, 262 (1949).
2) N. Lichtenstein, *J. Am. Chem. Soc.*, **64**, 1021 (1942).
3) Y. Sakato, T. Hashizume and Y. Kishimoto, *J. Agr. Chem. Soc. Japan* (*Nippon Nogei Kagaku Kaishi*), **23**, 269 (1949).
4) T. Hashizume, ibid., **25**, 25 (1951).
5) Y. Tsuchiya, Japanese Pat. Pub. No. 27-3417 (1952).
6) J. Edelson, C. G. Skinner and W. Shive, *J. Med. Pharm. Chem.*, **1**, 165 (1959).
7) G. B. Kline, U.S. Pat. 2873294 (1959).
8) Y. Tsuchiya, Y. Yamada and M. Sakurai. Japanese Pat. Pub. No. 37-11661 (1962).
9) M. Siegfried and O. Wiedenkanpt, *Z. physiol. Chem.*, **70**, 152 (1910).

*1 This specimen of ethylamine was prepared by the distillation of a commercial 70% aqueous solution in the presence of sodium hydroxide pellets. If 70% ethylamine is used, the main product will be pyrrolidonecarboxylic acid instead of theanine.

*2 A Rudolph photo-electric polarimeter, model 200, was used.

10) R. Boissonnas, German Pat. 1080113 (1960).